



Research Into Treatment-Resistant Constipation in Children

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International Foundation for Gastrointestinal Disorders (www.iffgd.org)

Reading time: 6 minutes

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Dr. Southwell is the recipient of the **IFFGD 2005 Research Award to Pediatric Investigator, Basic Science**. She has brought her skills in basic neurogastroenterology to understanding the causes of functional disturbances of colonic motility in children. She has also been coordinating a critical evaluation of a method to overcome constipation and soiling. Dr. Southwell aims to use multidisciplinary approaches to understand events that occur in normal and disease states, to provide a basis for effective treatment.

Constipation and fecal soiling in children and teenagers are major impediments to education. Schools will not accept children who cannot toilet themselves. Children whose soiled clothing gives off an odor are ostracized by others. Ten percent of 10 year old children have soiling. Paradoxically, 90% of children with soiling have constipation with bypass soiling (functional fecal retention and encopresis). Most of these children will respond to changes in diet and laxatives, but in 1 out of 200 constipation is not responsive to treatment and continues into adulthood.

Six Point Plan for Treatment-Resistant Constipation

We have developed a 6-point approach to treating children with chronic constipation:

- 1. Identify treatment-resistant constipation.** Initially we treat children with chronic constipation with changes in diet, with laxatives, and with pelvic floor training to separate responders and the children with treatment-resistant constipation.
- 2. Transit study to subgroup by site of slowing.** Chronic constipation can be:
 - Due to defects at the anus causing outlet obstruction,
 - Due to weak propulsion in the proximal colon,
 - Due to psychological or behavioral factors,
 - Associated with other organic or metabolic defects.Transit of food through the intestine is commonly followed using plastic markers. Food can be followed using a radioactive tracer. Children drink a small radioactive drink and movement of the drink is followed

by taking images of the abdomen every few hours (nuclear transit study or scintigraphy – an imaging method in which a mild dose of a radioactive substance is swallowed that shows how material moves through the GI tract). Using the nuclear transit study, we can separate children with outlet obstruction from those with weak propulsion in the proximal colon and those who can push food through at a normal pace. We also use clinical assessment and blood tests to determine if there is any underlying metabolic, genetic, or other identifiable defect that can cause constipation.

- 3. Disimpaction using appendix stomas with antegrade washouts.** We have developed a surgical method to prevent impaction (a hard mass of stool) of the bowel. To provide an access point at the top of the large bowel, a stoma (hole through the skin into the intestine) is created using the appendix. In a small operation, the appendix is brought out through the body wall, the end of the appendix is snipped off, and the open end of the appendix is sewn onto the belly wall. A special trapdoor button is inserted to close off the hole in the appendix and the wound is allowed to heal. The children and caregivers then insert a tube through the trapdoor into the bowel and can add laxatives directly into the colon. This produces a washout with the stool expelled through the anus. This is called an antegrade continence enema (ACE). We have 45 children with appendix stomas performing ACE at home. These children can attend school, and play sports, like gymnastics and football/soccer.

We are reviewing children with appendix stomas, Chait buttons and ACE to determine quality of life changes and their happiness with results, using a telephone questionnaire and age-relevant, bowel related questions.

- 4. Internal pressures in the colon.** We have developed a method to measure pressures inside the large bowel. We can use the appendix stoma to access the large bowel with no pain and no need for anesthetic. A special tube with sites that measure pressures (multi-channel manometry catheter) is fed into the appendix stoma and

along toward the anus. Once it has moved around the bowel, we connect it to a special machine that measures the pressures and records them onto a computer. We are able to measure pressures inside the bowel for 24 hours. By comparing the pressures to measurements from normal young adults, we can determine if the pressures are weak and where the weakness occurs. Our initial study on 5 children showed that they have reduced numbers of propagating contractions (colonic contractions that move fecal material through the colon to the rectum) pushing towards the anus. We are measuring pressures in a larger number of children and comparing children with slow colon transit to children with outlet obstruction.

5. **Viewing the nervous system inside the bowel.** We have developed surgical methods to collect 4 small biopsies of colon muscle from different sites along the bowel of children with weak propulsions. These biopsies are fixed and stained for molecules that label particular nerves that control muscle contraction and relaxation. We stain for 3 transmitter molecules and a marker for another special cell type (interstitial cells of Cajal) that are involved in muscle contraction and nerve to muscle transmission. Studies on a small number of children showed that certain nerves (Substance P nerves) are reduced in up to half of the children with weak colonic propulsions. We are performing a larger quantitative study on samples from 50 children with slow colon transit, 20 with outlet obstruction, and 30 adults with cancer to determine if lack of particular nerve populations is associated with poor propulsion.

6. **TICTOC – Resetting the colonic clock using**

electrical stimulation. [TICTOC = Transcutaneous Interferential Current To Overcome Constipation] Our physiotherapists have many years experience in urinary incontinence and have used a method of electrical stimulation to treat bladder weakness. They place suction electrodes on the skin near the groin and stimulate. They observed that some children developed diarrhea and decided to try a modified version of the method to overcome constipation. We have been excited to find that the method overcomes constipation and stops soiling. We have tested the method on 8 children. Five of the eight started passing stool normally and all stopped soiling. The effects last between 1 month and 3 months. We need to test the method on a larger group of children.

We need other groups to repeat our studies to determine how widespread chronic treatment-resistant constipation is and if they can be helped by the methods we have developed.

Studies On The Nervous System Controlling The Gut

As well as working directly with children, I do laboratory studies to understand the chemical structure of the nerves in the intestine. These studies help us to understand the function of different nerves and to develop methods and expertise to support the studies on human intestinal dysmotility.

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