

### Acid Suppression and Change of Gastric and Lung Microflora in Children

Acid suppression medications, such as H<sub>2</sub> receptor antagonists (H<sub>2</sub>RA) and proton pump inhibitors (PPI), are widely used medications in children. The long-term effect of such medications on microflora in the pediatric patient population is unclear. In this study, children who presented to a tertiary United States children's hospital with a complaint of chronic cough underwent evaluation of gastric and lung fluid cultures in a prospective manner. Chronic cough was defined as a cough that occurred at least 3 times per week for at least one month per year, and children with or without a history of acid suppression therapy were enrolled in the study. All children had received acid suppression medication for a minimum of four weeks, and sterile cultures were obtained by bronchoscopy (to obtain lung fluid) and esophagogastroduodenoscopy (to obtain gastric fluid). Probes with multichannel impedance / pH capability were obtained in children at the discretion of the investigating physician.

A total of 99 children were included in the study in which 51 children received no acid suppression medication while 48 children were on such medication (3 received H<sub>2</sub>RA; 45 received PPI). Children receiving acid suppression therapy had significantly more bacterial growth in the stomach (46%) compared to children receiving no medication (18%). Children receiving acid suppression therapy had a higher bacteria concentration in the gastric fluid, including pathogens such as *Staphylococcus* and *Streptococcus*. On the other hand, lung fluid obtained by bronchoalveolar lavage showed no significant difference in bacterial growth in children regardless of acid suppression medication status. Correlation matrices demonstrated that *Corynebacterium* and *Propionibacterium* were significantly more likely to be in the gastric and lung fluid of children receiving acid suppression therapy. In the children who had undergone pH / impedance monitoring, study subjects with non-acidic proximal channel reflux had a significantly higher concentration of lung concentration of several bacteria, including *Bacillus*. No such correlation was seen with acidic

reflux. No specific acid suppression medication dosing (milligram/kilogram dosing) could be correlated with bacterial growth in the stomach or lung.

This study demonstrates that acid suppression therapy in children is correlated with bacterial growth in the stomach. Also, acid suppression therapy appears to be associated with non-acidic reflux which theoretically increases bacterial concentration in the lungs. There is a risk of bacterial growth in the stomach and lungs in children receiving long-term acid suppression therapy, and the effect on lung remodeling as well as the effect on immune compromised children is unknown.

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Rosen R, Amirault J, Liu H, Mitchell P, Hu L, Khatwa U, Onderdonk A. "Changes in gastric and lung microflora with acid suppression: acid suppression and bacterial growth." *JAMA Pediatrics*. 2014; 168: 932-937.

### Is There a Biologic Link to Childhood Feeding Problems?

Pediatric gastroenterologists often are involved in the evaluation of children with feeding problems, and commonly, no etiology is found although many children improve clinically over time. The authors of this study looked at a specific set of patients with Smith-Lemli-Opitz Syndrome (SLOS) (OMIM #270400) which is associated with multiple congenital abnormalities (head and neck, cardiovascular, kidney, and orthopedic) as well as severe feeding issues. SLOS is autosomal recessive and has been found to be associated with disordered cholesterol synthesis in which a correlation exists between low cholesterol, high levels of 7-dehydrocholesterol (7DHC) and aggressive behavior. The authors of this study tried to determine if a correlation also existed between these biochemical perturbations and the feeding problems associated with SLOS.

Twenty-six children with SLOS and elevated 7DHC levels were evaluated multiple times over 6 to 12-month intervals. A panel of 5 questions evaluating for the presence of dysphagia, gastroesophageal reflux, aspiration, oral feedings, and use of gastrostomy assessed severity of each child's feeding problem while a SLOS anatomic severity score was also used to assess abnormalities such as cleft lip, palate, and uvula. Feeding assessments were determined by following

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the American Speech-Language-Hearing Association guidelines. Although most patients received cholesterol supplementation as part of their therapy to correct hypocholesterolemia, 20 patients were placed on a low cholesterol diet given over 3 weeks to evaluate cholesterol / 7DHC changes over time in relation to their underlying feeding problem.

Gastrostomy placement was performed in approximately 38% of patients while failure to thrive was present in 50% of patients. A direct correlation was seen between the severity of feeding problems and high 7DHC levels while an indirect correlation was seen with low cholesterol levels. The strongest correlation existed between 7DHC levels and degree of feeding impairment by scoring, especially in relation to oral motor function. Elevated 7DHC levels also were associated with gastrostomy use. No association was seen between 7DHC levels, cholesterol, and anatomic abnormalities suggesting 7DHC levels were not affecting anatomic abnormalities. Additionally, no association was seen between current 7DHC levels

and feeding impairment suggesting that cholesterol supplementation did not improve underlying feeding problems seen with SLOS. Patient age was associated with improved feeding regardless of 7DHC levels although many SLOS patients may have improved with feeding as they became older for reasons that are not fully elucidated.

The authors suggest that 7DHC levels are a possible marker of feeding difficulty in children with SLOS. Furthermore, these results raise the intriguing idea that yet unknown biochemical abnormalities may exist for other children with feeding delay.

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Merkens M, Sinden N, Brown C, Merckens L, Roulet J, Nguyen T, Steiner R. "Feeding impairments associated with plasma sterols in Smith-Lemli-Opitz syndrome." *The Journal of Pediatrics*. 2014; 164: 836-841.

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John Pohl, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*

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