Setting the Pace for Gastroenterology Research and Clinical Innovation
DEAR COLLEAGUES,

We are excited to present this summary of research and clinical advances in Gastroenterology, Hepatology and Nutrition at Nationwide Children’s Hospital. When I came to Nationwide Children’s in 2004, I joined a well-established division poised to take its place among leading national programs. Looking back at what we have achieved since then, I feel confident that we have fulfilled our potential.

With more than 15,000 patient visits and more than 2,000 procedures performed each year, GI continues to be one of Nationwide Children’s fastest-growing programs. Our faculty has grown to number 23 pediatric gastroenterologists, many of whom are conducting leading pediatric research. The Center for Digestive Disorders, which was completed in 2008, is a national model for pediatric gastroenterology. U.S. News & World Report continues to recognize us among the top digestive disorders programs in the country.

The information presented here tells more of our story. We are sharing the updates not only in our clinical programs, but also the important research taking place at Nationwide Children’s, and within The Research Institute at Nationwide Children’s Hospital.

On behalf of the pediatric specialists and the rest of our clinical and research team, I invite you to learn more about our program and people. As always, we welcome collaboration with primary care practices and pediatric specialty programs, so please contact us at any time.

Sincerely,

Carlo Di Lorenzo, MD
Division Chief
Gastroenterology, Hepatology and Nutrition
Nationwide Children’s Hospital
Advanced research and clinical programs are making dramatic differences for children from across the U.S. and around the world.
An Advanced Facility for Advanced GI Care

Located on the main campus at Nationwide Children’s, the Center for Digestive Disorders is an advanced facility dedicated to the early detection, treatment and prevention of gastrointestinal disorders.

All components of the Center exist in contiguous space, designed by our GI faculty and staff. It features a contemporary design that utilizes the latest technology, while creating an environment committed to family-centered care. Highlights of the center include:

- An inviting family waiting and registration area
- Private consultation/education rooms
- Comfortable, child-friendly examination rooms
- Motility suites with viewing rooms
- Pre-operative/recovery area dedicated to GI patients
- Advanced GI procedure rooms
- Live video connection to procedure room for medical teaching
- Dedicated post-anesthesia care unit (PACU)

Take a virtual tour at NationwideChildrens.org/GI.

Center For Digestive Disorders

World-Class Leadership In Pediatric Digestive Disorders

The Division of Gastroenterology, Hepatology and Nutrition provides comprehensive patient care for a broad range of gastrointestinal, liver and nutritional problems. We excel in research, teaching and clinical care, and maintain a team of physician-scientists committed to the creation of new knowledge in the discipline.

Our gastroenterologists are highly trained pediatric physicians who are skilled in the full range of digestive and liver diseases and disorders, and dedicated to the highest level of care. Each physician specializes in a particular area of the digestive tract, providing our patients with in-depth knowledge and understanding of their conditions. These physicians work as a team with pediatric nurse practitioners to diagnose and treat gastrointestinal diseases and disorders, while collaborating with other specialists, such as dietitians and behavioral and developmental psychologists, to provide comprehensive, coordinated care for each child.

With more than $5 million in external research funding relating to gastroenterology, hepatology and nutrition, Nationwide Children’s is a national leader in the generation of new knowledge relating to these fields. Our GI program has a long history of contributions to scientific laboratory, clinical and translational research, and continues to be on the cutting edge of research in a broad array of areas.
Our pediatric experts give new hope to children with motility disorders.

The Motility Center at Nationwide Children’s leads the nation in the expert care of children with motility disorders. From behavioral-related motility problems to complex abnormalities of the enteric nervous system, our motility experts are pioneering innovative tests and treatments to give families new hope for their children.

We diagnose motility problems using advanced techniques, including antroduodenal and colonic manometry, wireless motility capsule, esophageal impedance, electrogastrography, gastric and colonic scintigraphy, and electronic barostat. These specialized methods study how the intestine moves, contracts and relaxes. They can also measure intestinal perception, including the threshold for discomfort and pain from the intestine.

GASTRIC PACEMAKERS

Gastric pacemakers have been used in adults with gastroparesis, but Nationwide Children’s was one of the first to utilize the therapy to help children. The pacemaker is inserted into the abdomen, with electrical wires leading to the stomach. After the patient eats, the system stimulates the stomach with electrical impulses triggering it to empty.

Prior to laparoscopic placement of the device, a temporary pacemaker is placed endoscopically and clipped to the mucosa of the stomach. If symptoms improve, the decision is made to proceed with the permanent pacemaker.

CASE STUDY

Profile: Emma was first evaluated for persistent vomiting with feeding intolerance in 2005. She was found to have delayed gastric emptying – gastroparesis. Gastrojejunal (GJ) feedings were initiated, but she continued to have persistent vomiting and bloating. Her condition kept her from attending school and left her with little social life, because she was constantly vomiting and extremely bloated. Emma subsequently failed therapeutic trials using metoclopramide, erythromycin, tegaserod and ondansetron, and was referred to Nationwide Children’s.

Treatment: After extensive testing, medication trials and dietary interventions, Emma became a candidate for gastric electrical stimulation therapy and was the first patient to receive the GI pacemaker at Nationwide Children’s.

Outcome: Since the insertion of the pacemaker, Emma’s nausea and vomiting have resolved and she is able to eat. She receives follow-up care for device adjustments, evaluations and nutritional guidance.
RUMINATION SYNDROME
Rumination syndrome is sometimes confused with other gastrointestinal problems. Patients are usually healthy until an intercurrent event triggers the symptoms of rumination. Typically, the symptoms last several months or years before a diagnosis of rumination is made.

Gastroenterologists at Nationwide Children’s use the Rome III Criteria, often in combination with antroduodenal manometry, to accurately diagnose the disorder. Once diagnosis is confirmed, the patient enrolls in a two-week inpatient program. The inpatient program provides the opportunity to:

- Manage medications
- Monitor nutritional and hydration status
- Gradually transition from supplemental feeds to oral feeding
- Focus on the behavioral aspects of rumination syndrome
- Involve several disciplines in its management on a daily basis

Once patients successfully complete the program, they have the skills to self-manage the disorder.

CASE STUDY
Profile: A 14-year-old female presented with recurrent vomiting, which began at a time she had focused on losing weight. Vomiting after meals resulted in J-tube placement to support nutrition and hydration. Clinicians noted the vomiting pattern appeared unusual, occurring typically immediately after eating and sometimes while speaking.

Antroduodenal manometry testing at Nationwide Children’s identified post-prandial rumination waves associated with emesis of ingested foods. The patient was admitted to our inpatient rumination treatment program. Observation suggested the patient tended to eat quickly. Within 10 minutes of starting to eat, she described feeling pressure and that the food was “coming up.”

Treatment: The patient’s treatment included education about rumination, and awareness training to recognize signals of impending rumination and abdominal contractions. She received biofeedback training, which included slower, diaphragmatic breathing to reduce sympathetic nervous system activity both during and after mealtime.

Meal structure emphasized slower intake of gradually larger amounts with the goal of keeping the food down and re-swallow any food that came up. Training focused on gradually increasing tolerance and managing discomfort. In addition to psychology and gastroenterology, her day was structured with therapies including massage, therapeutic recreation and child life – all sharing the common goal of symptom management.

Outcome: After eight days, the patient could retain enough nutrition to maintain weight and hydration, without supplementation. Occasional rumination occurred, but did not result in expulsion of food or fluid. Post discharge, the patient had renewed energy and enjoyed regular activities. Subsequent checkups showed she had grown in height and had maintained her weight.


Pediatric gastroenterologist Desale Yacob, MD (left), and pediatric psychologist Anthony Alioto, PhD, represent two of the key disciplines in treating rumination syndrome in children and adolescents.
Motility Disorders (continued)

We are breaking new ground in motility therapies and research.

Nationwide Children's is one of the few hospitals in the country utilizing the following innovations in the study and treatment of motility disorders.

Motility Capsule Clinical Study
A less invasive but informative test involves the use of a wireless motility capsule, which is the size of a vitamin. When swallowed, the capsule passes through the intestinal tract, while transmitting helpful information and measurements, including transit times, acidity (pH) and pressures. These measurements are then used to determine how long it takes for food to leave the stomach.


Ultrasonography for Gastric Function
Using ultrasonography data on gastrointestinal disturbances in adolescents with anorexia nervosa, our researchers found that these patients do not have delayed gastric emptying, but do experience impaired gastric accommodation, which improves after nutritional rehabilitation. In addition, these adolescents meet more criteria for functional gastrointestinal disorders, which also become less common after nutritional rehabilitation.


Nuclear Medicine for Colonic Transit
Our groundbreaking research includes the use of nuclear medicine to study how the colon works. Scientists at Nationwide Children's have learned that colonic scintigraphy is a well-tolerated procedure, which can yield data comparable to other diagnostic procedures currently used for the categorization of the type of colonic dysfunction in constipation. Because it's better tolerated, it may be a more useful tool in evaluating pediatric patients with severe constipation.


Sacral Nerve Stimulation for Fecal Incontinence
Sacral nerve stimulation is a promising new therapeutic modality for children with fecal incontinence secondary to colonic dysmotility. The two-stage procedure involves a test phase followed by permanent implantation of the electrical stimulator, if the patient experiences significant improvement in fecal incontinence during test stimulation. The sacral nerve stimulator helps to restore normal nerve activity, so that children with fecal incontinence can defecate normally.

Effect of Amoxicillin-Clavulanate on Gastrointestinal Motility in Children
The goal of this study was to examine whether the common antibiotic, amoxicillin-clavulanate, might serve as a new option for treating upper gastrointestinal tract motor function. The study showed that amoxicillin-clavulanate triggered groups of propagated contractions within the small intestine, similar to those observed during the duodenal phase III of the interdigestive motility process.

Inflammatory Bowel Disease

Our multidisciplinary approach has produced some of the highest remission rates in the U.S.

The nationally recognized IBD Center at Nationwide Children’s uses a specialized, multidisciplinary approach to provide expert, comprehensive care for children with Crohn’s disease and ulcerative colitis. The Center provides intensive support for each patient through clinical management, patient and family education, dietary guidance and counseling. In addition, we strive to increase the collective knowledge of diagnostics and treatment through research.

ImproveCareNow

Nationwide Children’s is a leader in ImproveCareNow, a pediatric IBD collaborative that includes 55 children’s hospital sites. The aim of ImproveCareNow is to improve the management and care of patients with inflammatory bowel disease through the use of quality improvement methodology.

The principles learned and developed in conjunction with ImproveCareNow have been integrated into our IBD program. Likewise, the successful tools and processes developed here have been shared with ImproveCareNow and, as a result, have been implemented by other sites across the country. Through the use of these quality improvement methods, we have seen improvements in a variety of process and outcome measures, most notably an increase in clinical remission rates from a baseline of approximately 50 percent to 84 percent currently, one of the highest rates in the network – giving our patients one of the highest rates of remission in the country.

Sandra Kim, MD, and Wallace V. Crandall, MD, lead the IBD Center, a national model for quality initiatives that lead to dramatically improved outcomes.
**IBD CASE STUDY**

**Profile:** A 14-year-old female presented with abdominal pain, weight loss and anemia. Upper endoscopy and colonoscopy revealed significant inflammation of the terminal ileum and colon. These findings and subsequent biopsy results confirmed Crohn’s disease. She was started on immunosuppressive medications, including prednisone and 6-mercaptopurine. (See examples of normal and diseased terminal ileum and cecum.)

**Treatment:** While the patient made some clinical improvement, signs of active disease persisted. During pre-visit assessment, she was noted to have persistent anemia and nutritional failure. Evaluation by our IBD nutritionist was scheduled, and the new concerns were brought to the attention of her GI physician. Modification of her treatment plan, including the addition of nutritional supplements, was recommended.

Because of her ongoing, active disease, this case was reviewed during the weekly population management meeting. A pattern of medication non-adherence and missed appointments was noted. Evaluation and therapy recommendations were provided. Subsequent discussion with the family revealed that financial limitations, unreliable transportation and anxiety were impacting her clinical care. The IBD social worker assisted with these concerns. The patient began to work with our IBD psychologist in dealing with her stressors and anxiety. She was also successfully changed to, and was adherent with, infliximab therapy as recommended, resulting in sustained clinical remission of her disease.

**Outcome:** Our ability to carefully review this case outside the busy clinic setting, using pre-visit planning and population management, allowed for rapid identification of clinical concerns. The IBD social worker helped analyze the cause of the patient’s issues, and appropriate interventions were made that resulted in a substantially better outcome than she might have otherwise experienced. The patient successfully advanced to biological therapy with improved control over her disease and then entered a period of sustained remission.

**RESEARCH HIGHLIGHTS FROM THE IBD CENTER**

Research is critical to improve patient outcomes. IBD Center investigators are at the forefront nationally in efforts to understand how we can better deliver care for children and teens living with IBD. Researchers are examining the effects of current treatments, while searching for alternatives, including novel therapeutics not offered in most pediatric centers. They are also investigating how IBD patients adjust behaviorally, emotionally and socially to their disease and how psychosocial factors impact symptom severity.

Wallace Crandall, MD, Director of the IBD Center and Associate Medical Director for Quality Improvement at Nationwide Children’s, has published extensively on IBD and quality improvement. Dr. Crandall serves on the Executive Committee and as Director of Quality for ImproveCareNow, and on the steering committee for the CCFA Pediatric IBD Research Network (PRO-KIIDS). He is also the past chair of the NASPGHAN IBD Committee, past co-chair of the NASPGHAN Quality Improvement Task Force, as well as a past member of the CCFA Pediatric Affairs and National Scientific Advisory Committees. His research, focusing on improving treatment options and the quality of care for patients with IBD, has been funded by the CCFA, NIH, and AHRQ.

Laura Mackner, PhD, psychologist and investigator in the Center for Biobehavioral Health, is a nationally recognized expert in the psychosocial aspects of chronic illness in children and adolescents, particularly in those living with IBD. Her current work, which is funded by the NIH, explores biopsychosocial issues in adolescents with IBD, peer-to-peer mentoring and socially interactive technology use in this population.

Sandra C. Kim, MD, medical director of the IBD Center, studies pediatric IBD, with a focus on adolescent transitioning, quality improvement, and the impact of the gastrointestinal microbiota in IBD. Her research has been funded by the NIH and the Crohn’s and Colitis Foundation of America (CCFA). Dr. Kim is chair of Pediatric Affairs for CCFA, and serves as a member of the Executive Committee for the CCFA National Scientific Advisory Committee and the steering committee for the CCFA Pediatric IBD Research Network (PRO-KIIDS). In addition, she chairs the Clinical Practice and Adolescent Transitioning committees for ImproveCareNow. She also is a councilor for the American Gastroenterological Association (AGA) Immunology, Microbiology, and IBD (IMIBD) section.

Brendan Boyle, MD, MPH, a pediatric gastroenterologist and researcher, is currently investigating development of reliable and consistent care delivery systems to improve the quality of patient care. On a national level, Dr. Boyle serves as a member of the NASPGHAN IBD and CCFA/NASPGHAN website committees.

Jennifer Dotson, MD, MPH, a pediatric gastroenterologist and principal investigator in the Center for Innovation in Pediatric Practice in the Research Institute at Nationwide Children’s, conducts clinical research in comparative effectiveness, and outcomes-based research in pediatric IBD. Dr. Dotson is a recipient of the prestigious NASPGHAN Crohn’s and Colitis Foundation of America Young Investigator Career Development Award.

Wallace V. Crandall, MD, and Laura M. Mackner, PhD, study the psychological and social aspects of adolescents with IBD.
Our Pediatric Polyposis Program identifies at-risk patients to save lives.

For those with polyposis disorders, regular endoscopic surveillance of the digestive tract is an important tool in controlling cancer risk. The development of early and recurrent colorectal cancer is a reality for many families that carry a genetic mutation. Early identification of the child at risk allows for better surveillance and counseling with the goal of controlling cancer risk and improving quality of life. The Pediatric Polyposis Program at Nationwide Children’s focuses on identifying and controlling the disease process.

Pediatric gastroenterologist Steven H. Erdman, MD, has built a national reputation caring for children and adolescents with hereditary polyp disorders and colorectal cancer syndromes. Dr. Erdman is also one of the few specialists in the United States with expertise in using double balloon enteroscopy as a diagnostic and therapeutic procedure with pediatric patients.

TECHNOLOGY HIGHLIGHTS

Double Balloon Enteroscopy (DBE)
The small intestine was previously inaccessible by standard endoscopic techniques due to the length of the digestive tract and its free-floating nature. But unique procedures like double balloon enteroscopy (DBE) changed all of that. DBE allows for direct visualization of the entire small intestine with the ability to obtain biopsies if abnormal areas are found, to remove polyps, or to treat a bleeding site.

When our pediatric gastroenterologists began using DBE in 2006, it was a relatively new technology that had not been adapted for use in pediatric patients. We continue to be one of only a few institutions in the U.S. with both the equipment and expertise in using DBE in pediatric patients.

Capsule Endoscopy
Our pediatric gastroenterologists have unique expertise in the use of noninvasive capsule endoscopy as an important diagnostic tool in pediatric patients. Capsule endoscopy allows for visualization of the lining of the small intestine in areas of the intestine that cannot be seen with standard endoscopy. This can be helpful in evaluating problems, such as identifying a source of bleeding in the small intestine, further evaluation of IBD, or looking for polyps or other lesions in the small intestine.

Capsule endoscopy is also a powerful diagnostic tool when used in combination with DBE. Nationwide Children’s is one of the few pediatric hospitals using capsule endoscopy with DBE in the care of children and adolescents and these techniques have been used in a number of successful cases from across the country.

Steven H. Erdman, MD, is a leading national specialist in diagnosing and caring for children and adolescents with hereditary polyp disorders and colorectal cancer syndromes.
Polyposis and Colon Polyps in Children (continued)

POLYPOSIS CASE STUDY

Profile: A 13-year-old female was referred due to recurrent polyp development in her duodenum. Her local pediatric gastroenterologist had been able to control the polyps in the stomach and colon by upper endoscopy and colonoscopy, however there was concern over possible polyp growth in the small intestine. When biopsies of the lesions in the upper duodenum showed high-grade dysplasia, the child was referred to Nationwide Children’s.

In addition to recurring GI polyps, the child had developmental delay, macrocephaly and other disorders, the result of chromosome 10q23 deletion syndrome, which placed her at significant risk of developing adenocarcinoma throughout the GI tract at a very early age.

Diagnosis: Following an initial clinic visit, a follow-up esophagogastroduodenoscopy was done with recovery of entire polyps by snare polypectomy and deployment of the endoscopic capsule. Due to her developmental disabilities, she was unable to swallow the capsule and direct deployment into the duodenum avoided risk of the stomach retaining it.

Treatment/Outcome: Capsule endoscopy study revealed several large irregular polyp-like structures in the duodenum and upper jejunum with the rest of the jejunum and ileum showing no abnormalities. DBE was performed and located four large irregular pedunculated polyps in the upper jejunum. (See Image 1a.) The polyps were removed using a polyp snare and electrocautery. Due to the limitations of the duodenum. (continued)

an additional 200 cm into the small intestine to confirm the absence of other polyp lesions. Upon reaching the farthest depth in the small intestine, a small India ink mark was left in the wall of the proximal ileum at the further point of the current study. This mark will be an important landmark if future capsule or DBE studies are needed. (See Image 1b.)

Fortunately, histologic examination showed the polyp lesions had no evidence of dysplasia or early malignant transformation. By avoiding major surgery, this patient was able to drink liquids the evening of the procedure and left the hospital the following morning. As part of a surveillance plan, the combination of these procedures will be used in the future for this patient to monitor any further polyp development.

POLYPOSIS RESEARCH

Polyposis is known for its unpredictability. Genetic mutations in two genes (BMPR1A and SMAD4) have been linked to roughly half of the families with juvenile polyposis syndrome, meaning other causative genes remain to be identified.

Research by gastroenterologist John Barnard, MD, is shedding light on how gastrointestinal diseases develop and evolve at the molecular level. His work on tumor growth will contribute to a more thorough understanding of the development of the GI tract and the origin of intestinal polyps.

While the focus of Dr. Barnard’s research is the biology of intestinal development, the work of gastroenterologist Steven H. Erdman, MD, centers on new interventions for GI disorders. Specifically, he is using advanced techniques to treat existing GI polyps and hereditary cancer syndromes in children. Dr. Erdman is one of the first pediatricians in the country to use double balloon enteroscopy in the treatment of children with diseases of the small intestine and has published peer-reviewed articles regarding this pediatric perspective.

RECENT FINDINGS

ZAS3 Accentuates TGF Beta Signaling in Epithelial Cells

Investigators identified an interaction between ZAS3 and Smad proteins that enhances TGF beta signaling, suggesting that ZAS3 plays a functional role in TGF beta signaling. TGF beta is a protein that controls cell proliferation in normal epithelial cells and at early stages of tumor development, including intestinal tumors.


Double-Balloon Enteroscopy: Pediatric Experience

To shed light on the indications and possible benefits of double-balloon enteroscopy (DBE) in children, physicians from Nationwide Children’s reviewed the outcomes of DBE cases performed at the hospital during a two-year period. Study results indicated the use of device-assisted enteroscopy, such as DBE, to conduct complete examination of the small bowel, may be just as successful in pediatrics as it has been in adult medicine. The use of this technology can benefit diagnostic and treatment capabilities of polyposis and other GI conditions.


Review: Clinical Features of the Three Most Common Polyp Syndromes of Childhood

Colon polyps are a common finding in pediatrics. However, when polyps are present in greater numbers, or are associated with a family history of polyps, or colon or other cancers, a polyposis or hereditary colorectal cancer syndrome should be considered. This article reviews the clinical features and provides updates on the three most common hamartomatous polyp syndromes of childhood: juvenile polyposis syndrome, Peutz-Jeghers syndrome, and the PTEN hamartoma tumor syndrome.

Our one-of-a-kind programs approach feeding disorders from a multi-organ perspective.

NEONATAL AND INFANT FEEDING DISORDERS PROGRAM
This unique program, developed by Sudarshan Jadcherla, MD, FAAP, FRCP, DCH, AGAF, focuses on the diagnosis of gastrointestinal dysmotility mechanisms among high-risk infants. Infants with feeding difficulty receive crib-side tests including esophageal manometry, gastro-duodenal manometry, evaluation of oro-pharyngo esophageal motility, pH studies and pH-impedance studies. Oromotor stimulation methods are also applied to modify infant dysphagia. These studies help in the diagnosis, prognosis and identification of the mechanism of feeding difficulty. An infant disease-specific feeding practice algorithm is developed based on the mechanistic diagnosis and symptom correlation. A multidisciplinary treatment team then uses this algorithm to develop a patient-specific feeding plan. This program involves close collaboration with parents.

A study of this program involved 100 infants with severe complex feeding difficulties that were at risk for gastrostomy, and were evaluated through this program. Fifteen of the infants learned to feed by mouth and were sent home without the need for gastric tubes. Aside from the improved quality of life, these outcomes saved an estimated $2.1 million in health care costs for the participants through prevention of gastrostomy. Overall, the study concluded that short- and long-term feeding outcomes in complex neonates can be significantly improved through innovative feeding strategies at a reduced cost. Clinical and aerodigestive motility characteristics were predictive of outcomes.


Feeding Disorders
Renowned neonatal feeding specialist Sudarshan R. Jadcherla, MD, leads the Neonatal and Infant Feeding Disorders Program.
Feeding Disorders (continued)

FEEDING ENHANCEMENT PROGRAM
Dr. Jadcherla developed the Feeding Enhancement Program as an addition to the Neonatal and Infant Feeding Disorders Program. bedside rounds enhance educational and skill competencies of all feeding providers, including physicians, nurses, occupational therapists, lactation consultants, nutritionists and parents. The purpose of the feeding enhancement program is to streamline the feeding process to help neonates learn to feed sooner and with fewer complications. Interestingly, the feeding milestones are acquired sooner, length of hospital was lesser, and the overall patient care charges were lesser.

RESEARCH ADVANCES
Feeding disorders research at Nationwide Children’s focuses on understanding the mechanisms of feeding difficulty and improving short-term and long-term feeding outcomes in complex neonates and toddlers.

Discovery of Normal and Abnormal Mechanisms of Neonatal Feeding and Aerodigestive Reflexes
Successfully funded by the National Institutes of Health (NIDDK), Dr. Jadcherla is investigating the patho-physiological mechanisms involved in normal and abnormal feeding skills in neonates and high-risk infants. Normal feeding patterns involve the close interaction between the central nervous system, the enteric nervous system and airway reflexes. Dr. Jadcherla uses provocative manometry, high-resolution manometry and pH-impedance studies to visualize functional and dysfunctional mechanisms of feeding. These crib-side tests assess vagal nerve-mediated aero-digestive reflexes specific to each infant. Findings are used to develop personalized, safe enteral and oral feeding strategies, a key element of the Neonatal Feeding Disorders Program. Apart from allowing personalized treatment approaches, this cutting-edge research is helping to create a picture of feeding strategies, a key element of the Neonatal Feeding Disorders Program as an addition to the Neonatal and Infant Feeding Disorders Program.

Determining Normal and Abnormal Clinical Mechanisms of Neonatal Feeding Difficulty
Supported by two grants from the NIDDK, Dr. Jadcherla leads the investigation of basic integrative physiological mechanisms pertinent to normal and abnormal feeding skills in human neonates. Therapeutic strategies are based on crib-side tests to assess vagal nerve mediated aero-digestive reflexes, and include personalized safe enteral and oral feeding strategies. In a second study, the effect of an innovative diagnostic and management approach on feeding outcomes in infants referred for home-tube feeding methods was evaluated – it was shown that short- and long-term feeding outcomes were improved at a reduced cost. Future studies will involve simplification and improvement of feeding management, identification of co-morbid risk factors for chronic feeding disorders, and development of methods to minimize the variability in feeding strategies among providers.


Esophageal Disease in Pediatrics
A study on esophageal disease in pediatrics covers the acquisition of neuromuscular maturation; physiology of esophageal peristaltic and sphincteric reflexes; implications for clinical practice; and conditions that predispose patients to severe gastroesophageal reflux disease in children with potential risk for esophageal cancer.


Esophageal Sensation in Premature Human Neonates
Nationwide Children’s researchers examined the effect of visceral provocation on aerodigestive reflexes, electrocortical arousals and respiratory changes in premature neonates.


Study Helps Clarify Symptoms and Characteristics of Acid Reflux in Neonates
In the first study to classify reflux and its associated symptoms in neonates based on how and what is refluxed, researchers at Nationwide Children’s discovered that modifying stomach acid levels may not be enough to treat symptoms in neonates suspected of having gastroesophageal reflux disease.


Translating to Oral Feeds and the Role of Pain Control
Developing effective treatments to facilitate the transition from gastrostomy to oral feeding is a critical step in the health and care of our affected patients and their families. Hayat Mousa, MD, in collaboration with the University of Kansas Medical Center and Children’s Hospital of New Orleans, is leading a NIH-funded clinical trial to determine whether the use of amitriptyline is helpful in moving children from tube to oral feeding, and whether or not the treatment of pain helps with this transition. Participants, age 9 months to 9 years, will receive either amitriptyline or placebo once daily at bedtime for 24 weeks. After participating for 10 weeks, all children will receive a prescription for the appetite stimulant megestrol twice daily. The end goal is to develop new, long-term solutions to encourage children to eat orally.

Hayat Mousa, MD, is collaborating with other institutions in an NIH-funded clinical trial on use of amitriptyline in moving children from tube to oral feeding.
Our researchers take a focused look at GI genetics and developmental biology.

Despite advances in diagnostic, therapeutic and surgical care for gastrointestinal diseases, some remain difficult to treat. Understanding the genetic and biological mechanisms of these diseases will allow the development of improved treatments. Using genetic analysis, animal models and in vitro cell culture models, investigators at Nationwide Children's are examining how the gastrointestinal tract develops and how gastrointestinal diseases develop and evolve at the molecular level.

GI Genetics and Tissue Engineering
Cheryl Gariepy, MD, studies the development of the enteric nervous system (ENS), which controls movement, secretion and blood flow in the intestines. Her research also includes the causes of pediatric pancreatitis. Projects include:

- Using a variety of molecular biologic, histologic, physiologic and survival surgical techniques to understand the mechanisms controlling normal ENS development
- Investigating the therapeutic potential of transplantation of a tissue-engineered ENS
- Working with international experts on the steering committee of the Hirschsprung Disease Research Collaborative to identify gene mutations causing this ENS birth defect, improve and standardize its diagnosis and management, and comprehensively characterize clinical outcomes
- Examining the genetic causes, evaluation and treatment of recurrent and chronic pancreatitis in children with the NIH-funded international consortium, International Study Group of Pediatric Pancreatitis: In Search of a Cure (INSPPIRE)

Attacks Against the Enteric Nervous System, a Role in IBS
Researchers theorize that patients with irritable bowel syndrome (IBS) have abnormal intestinal motility and are hypersensitive to those changes. Gastroenterologist Jonathan Gisser, MD, believes that an attack on the enteric nervous system may cause these sensitivities. Dr. Gisser’s work involves:

- Testing blood samples from children with IBS and other GI disorders for antibodies against the ENS
- Determining if these antibodies are more common in kids with IBS
- Developing diagnostic tests and research to determine if blocking these antibodies could prevent IBS symptoms

Pediatric gastroenterologists Jonathan Gisser, MD, and Cheryl Gariepy, MD, conduct groundbreaking research into the intricacies of the enteric nervous system.
Necrotizing Enterocolitis

We are focused on protecting our most fragile patients from necrotizing enterocolitis.

Despite improvements in clinical care, necrotizing enterocolitis (NEC) remains the leading cause of surgical death among premature neonates. In collaboration with the Neonatal Research Network, one of the largest networks of clinical neonatal care in the U.S., the Center for Perinatal Research at Nationwide Children’s is poised to make significant improvements in the prevention of prematurity and reduction of complications associated with premature birth, such as NEC. Centers with the Neonatal Research Network participate in multi-center clinical trials and observational studies in neonatal medicine.

Studying HB-EGF, a Growth Factor to Protect and Heal the Intestine

After more than two decades of research, Gail Besner, MD, principal investigator in the Center for Perinatal Research and Chief of the Department of Pediatric Surgery at Nationwide Children’s Hospital, and her team have found that heparin-binding EGF-like growth factor, or HB-EGF, protects the intestines from multiple forms of intestinal injury including NEC. HB-EGF is a protein that stimulates cells to grow and to move. Cell proliferation and migration are critical to wound healing, including the healing of intestinal wounds. In addition, HB-EGF decreases production of multiple substances that are formed upon intestinal injury and that would normally act to worsen the injury. This allows the protein to protect the intestine from further harm. Having discovered the growth factor in 1990, Dr. Besner has published extensively demonstrating the intestinal cytoprotective effects of HB-EGF. She is funded by the NIH to study these effects.

Recent studies show administration of HB-EGF, in conjunction with stem cell therapy, acts synergistically to further protect the intestine from injury. Dr. Besner’s studies offer encouragement for a healthier future for premature babies. Newborns, especially those born prematurely, are at particular risk of developing NEC. Dr. Besner’s research suggests HB-EGF may hold significant clinical potential. The future goal is to determine whether administering it to very-low-birth-weight premature babies might prevent NEC from developing.

Poly(ADP-ribose) Polymerase-1: A Novel Therapeutic Target in Necrotizing Enterocolitis

Inflammation and oxidation may be involved in NEC. The enzyme Poly(ADP-ribose) polymerase-1 (PARP-1) is a key DNA repair enzyme, however, when oxidative stress and DNA damage happen, PARP-1 may over-activate and deplete cells of NAD+ and ATP, which kills the cells. Researchers speculate that PARP-1 overactivation in NEC may drive cell death in this disease and that PARP-1 may be a novel therapeutic target in NEC.

Intestinal Support Service

Our team approach improves quality of life for children with intestinal failure.

Caring for infants, children, and adolescents with short bowel syndrome and other forms of intestinal failure is a complex process. The Intestinal Support Service at Nationwide Children’s focuses on helping children reach the point where they no longer require either parenteral or enteral nutrition. For those in whom this is not possible, the focus is on maximizing their potential both in terms of intestinal function and in life as a whole. The multidisciplinary team strives to help these children and their families lead as normal a life as possible, even when they still require ongoing specialized nutrition support. This can only be accomplished by a committed team that includes gastroenterologists, surgeons, radiologists, nurse practitioners, nurses – including nutrition support nurses – dietitians, pharmacists, social workers and administrative support.

The Intestinal Support Service works closely together as a team, as well as with the child’s primary care physician and other pediatric subspecialists (medical and surgical). Collectively, the service provides coordinated care both at home and when the child needs to be in the hospital. The Intestinal Support Service is unique in this aspect – that when admission is required, the inpatient care is provided by this same team, led by Jane Balint, MD, and Molly Dienhart, MD, recognized experts in the field of intestinal rehabilitation. This allows for both continuity and consistency of care, which are essential elements for improving the outcome for these children. The team is structured with flexibility in mind, allowing for both routine and emergent care in the clinic, frequently preventing emergency room visits. Through collaboration with other experts in this field, the service provides highly effective, state-of-the-art strategies for minimizing liver disease and preventing blood stream infections – two major potential complications of intestinal failure.

Surgical specialists have expertise in operative management strategies such as bowel lengthening. In addition, the Intestinal Support Service coordinates with the Motility Center, allowing for more extensive evaluations of the intestinal tract when indicated, thus enabling the service to tailor the medical and surgical approach.
Liver Disease

Our faculty are focused on all aspects of liver disease.

The care of children with liver disease is complex and requires a well-coordinated effort among multiple specialists. Our comprehensive team includes physician specialists, registered nurses, dietitians, social workers, pharmacists, radiologists and pathologists. Our liver clinic follows a wide range of patients:

- Alagille syndrome
- Alpha-1 antitrypsin deficiency
- Biliary atresia
- Glycogen storage disease
- Hepatitis A, B and C
- Non-alcoholic fatty liver disease (NAFLD)
- Pre- and post-transplant patients
- Rare bile acid disorders
- Synthetic and transport defects
- Wilson’s disease

Fatty liver disease from obesity is becoming a major health issue in the U.S. We follow many patients with this diagnosis and work closely with Healthy Weight and Nutrition at Nationwide Children’s to treat this disease. We also work closely with the Teen Clinic in the diagnosis and management of acute hepatitis C from intravenous drug use.

RECENT FINDINGS IN LIVER DISEASE RESEARCH

Safety of Pediatric Percutaneous Liver Biopsy Performed by Interventional Radiologist

Although gastroenterologists are most commonly trained to perform percutaneous liver biopsies in children, interventional radiologists can perform this procedure equally as safe, according to our study, which appears in the Journal of Pediatric Gastroenterology and Nutrition, and is the first to report on these biopsies in U.S. children up to 21 years old.


Activation of CTGF-Transforming Growth Factor β 1 in HCV-Expressing Hepatocytes

Studies demonstrate a central role for CTGF expression in HCV-induced liver fibrosis and highlight the potential value of developing CTGF-based anti-fibrotic therapies to counter HCV-induced liver damage.


Immunotherapy of HCV with Antibodies against Programmed Cell Death-1

Findings suggest persistent HCV infection treated with anti-PD-1 antibodies may result in significant reduction in viremia, without apparent hepatocellular injury.


Carol Potter, MD, specializes in the unique needs of young patients with liver disease.
Leading Expertise in Childhood Celiac Disease

One of the foremost clinicians and researchers in childhood celiac disease, Ivor Hill, MD, leads the Celiac Disease Center. Dr. Hill has been instrumental in raising awareness of the disease in the U.S. Notably, he was the chair of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition committee that developed the first evidence-based guidelines on diagnosis and treatment of celiac disease in children. The Celiac Disease Center, one of the GI Division’s signature programs, provides comprehensive care to children and families affected by celiac disease. The multidisciplinary team includes pediatric gastroenterologists, endocrinologists, pathologists, pharmacologists, nutritionists, nurse practitioners, nurses and social workers.

GI Disorders in Children with Autism

While the connection between GI disorders and autism spectrum disorder is unclear, recent studies indicate that autistic behaviors are commonly found in children with constipation. Successful treatment of constipation and toilet training often require that these behaviors be taken into account in children with autism. Nationwide Children’s has developed an interdisciplinary, outpatient program that provides this unique focus.

The team of experts consists of pediatric professionals from a variety of disciplines, all of whom have experience and interest in working with children with autism spectrum disorders.

Team members include:
- Child life specialists
- Clinical dietitians
- Gastroenterologists
- Laboratory
- Nursing
- Pediatric nurse practitioners
- Psychologists
- Radiology
- Social workers

The core of this team approach is the specialized focus of pediatric psychologists who are vested in caring for children with developmental delays and autism spectrum disorders. Psychologists also perform testing at the Nationwide Children’s Child Development Center, which means our Autism Bowel Management Clinic patients are seen by providers who are trained to recognize their particular delay or disorder.

Pediatric gastroenterologist Kent Williams, MD, conducts basic and translational research into the mechanisms that cause functional gastrointestinal disorders, such as abdominal pain, constipation and reflux, in children with autism. He is an investigator at the Research Institute at Nationwide Children’s, and the Ohio State University College of Medicine and is funded by a K-award from the NIH.

Advanced Focus in Eosinophilic Esophagitis

Nationwide Children’s is taking a closer look at causes and cures of allergic inflammatory conditions of the esophagus. Elizabeth Erwin, MD, researches and practices in the areas of infectious diseases and allergy, and immunology, with a focus on understanding tolerance to allergens. She is the principal investigator on an NIH K-23 grant studying the change in allergen exposure and reversibility of the tolerant immune response.

Dr. Erwin has published on the topic of eosinophilic esophagitis (EoE) and brings her expertise, along with that of pediatric gastroenterologist John Russo, MD, to services provided within the GI Division.

The Eosinophilic Esophagitis program coordinates clinical care for children and adolescents by pediatric specialists within Gastroenterology and Allergy/Immunology. In addition, patients can participate in ongoing research studies to improve evaluation and treatment of EoE.


When your child needs a hospital, everything matters.

At Nationwide Children’s, we are creating the future of pediatric health care. We consider every detail. Every decision. Every aspect of the care we provide. From the child who comes to us with complex motility disorders, inflammatory bowel disease or polyposis. To those with a sprain, a broken bone, or a fever. Here, the future health and potential of all children is being shaped. Here, our doctors are revolutionizing each patient’s health and the health of future generations.

We are relentless in our pursuit of answers. Which is why our doctors are also researchers. And why we’re an international leader in pediatric research. Every question developed at the patient bedside has a place in the lab and someone there working passionately to answer it. Even doctors without research training work hand-in-hand with researchers.

We influence policies that change lives. We advocate for the rights of children in Ohio and around the world. We use research findings to impact how government officials develop laws protecting children. And we work tirelessly to make sure children’s voices are heard.

At Nationwide Children’s, everything matters to us. Because when it’s your child, or your patient, everything matters to you.

Referrals and Consultations

The Division of Gastroenterology, Hepatology and Nutrition at Nationwide Children’s accepts referrals from across the U.S. and internationally.

Online: NationwideChildrens.org  
Fax: (614) 722-4000  
Phone: (614) 722-6200 or (877) 722-6220  
Physician Direct Connect Line for 24-hour urgent physician consultations:  
(614) 355-0221 or (877) 355-0221

Take a video tour of the GI Center at NationwideChildrens.org/GI.

Ranked among the best children’s hospitals in all 10 specialties