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SPECIAL ARTICLE

A History of Pediatric Specialties

In the fifth article in this series, Drs. Walker-Smith and Walker describe the evolution of the specialty of pediatric gastroenterology. They make the point that the specialty evolved because of the perception of the special needs of children with gastrointestinal disease. They present not only the history of the advances in this field but also the many contributions of the clinicians and scientists whose work led to the establishment of this specialty. These experts developed societies, journals, and training programs providing, thereby, optimum care and study of children with gastrointestinal disease.

Alvin Zipursky
Editor-in-Chief

The Development of Pediatric Gastroenterology: A Historical Overview

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The rapid historic development of pediatric gastroenterology occurred in parallel in North America and Europe over the past four decades. Because the field is now becoming increasingly global, with more interaction among practitioners worldwide, the authors felt that the history of this discipline could best be considered from this dual perspective. However, it was felt to be important to begin by placing this development in its historic context.

The rise of pediatrics itself was intimately related to the establishment of children's hospitals in the 19th century (1). This need for specialization has been keenly debated by historians over the past 150 y and the perceived benefits of such a division of labor within medicine were often greeted by suspicion or frank hostility by many influential members of the profession, for example, Dr. Samuel Gee in London. Dr. Gee was a most distinguished physician who cared for both adults and children in the late 19th century. By his description of clinical entities in children such as celiac disease (2) and cyclical vomiting (3), he contributed to the rise of pediatrics and ultimately to pediatric gastroenterology. Yet he himself stated there are two medical terms he abhorred, the terms *specialist* and *consultant*. Although he made very important observations concerning diseases in children, which are central to pediatric gastroenterological practice, he can no way be regarded as a pioneer of the discipline itself.

However, by the beginning of the 20 century there was rapid change with the acceleration of the development of specialties and a wider appreciation of their value. At that time, most of the major specialties, namely medicine, surgery, gynecology, obstetrics, and, relatively late, pediatrics, had developed. The concept of organ-specific subspecialists such as gastroenterologists had also become established at the end of the 19th century. The first national gastroenterological society was founded in Germany in 1895 by Ismar Boas, the first physician to devote himself to gastroenterology (4). The American Gastroenterological Association was founded in 1897 in the office of Dr. D. Stewart (Philadelphia) along with seven other physicians (5). However, the pediatric organ subspecialties such as pediatric gastroenterology only began to emerge in the 1960s.

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Why did such pediatric subspecialties emerge? A simple answer to this question is urgent clinical need. The development of each of the pediatric subspecialties, as well as (in an earlier era) the development of pediatrics itself, was the result of the perception that children with special needs were receiving poor clinical care. Such a need had long been perceived. However, it was only when specialized techniques and resulting expertise in accurate diagnosis and effective treatment (which could expertly meet this need) had been achieved, that pediatric subspecialties emerged. By the early 1970s, such expertise had developed and the need for pediatric subspecialties became recognized in the United Kingdom (as well as in Europe and North America) by the pediatric community as a whole (6).

The particular catalyst for pediatric gastroenterology was the introduction of new diagnostic techniques that required special skills, and also the development of complex new therapies for children with gastroenterological disorders that required careful monitoring, particularly for their possible effect upon growth and development. The profound impact that many chronic gastrointestinal diseases have upon growth and the onset of puberty demonstrate that such children should be under the care of subspecialists trained to deal with gastrointestinal disease in children, rather than adult gastroenterologists. In addition, unique gastrointestinal conditions that specifically affected infants and were not seen in older children and adults, such as the inborn errors in bilirubin metabolism, digestive and absorptive genetic defects, the spectrum of metabolic liver disease, *e.g.* α-1-antitrypsin deficiency, etc., caused adult gastroenterologists to defer to their pediatric colleagues and for pediatricians trained in adult gastroenterology to be more in demand as consultants (7, 8).

MEDICAL EVENTS LEADING TO THE EMERGENCE OF PEDIATRIC GASTROENTEROLOGY

A summary of medical events leading to the emergence of pediatric gastroenterology is given in Table 1.

The development of the small intestinal biopsy was of particular importance in the emergence of pediatric gastroenterology (9), leading to an initial focus (in Europe, Australia, and Canada) on celiac disease. The observation by Dicke (10) in 1950 in Utrecht that celiac disease in children was effectively treated by a gluten-free diet was at first resisted in the United States but was readily accepted in Europe and Australia.

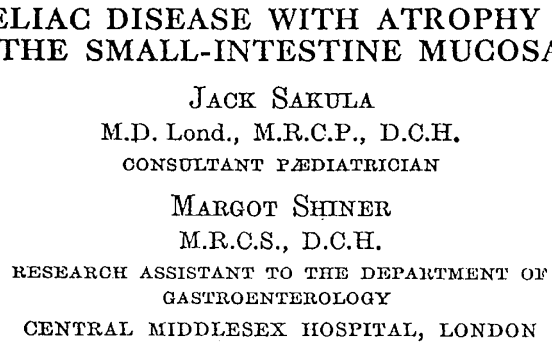
However, an adult gastroenterologist, Margot Shiner, made the first report of a small intestinal biopsy in a child with celiac disease (9). The 7-y-old child, she reported, had a flat small intestinal mucosa. This observation was published in *The Lancet* in 1957 with pediatrician Jack Sakula as co-author (9) (Fig. 1). It ushered in a whole new era, and from that time on many papers began to appear describing small intestinal mucosal lesions in children in a wide range of disorders.

Shiner, in fact, used a cumbersome rigid tube biopsy technique. It was the subsequent advent of the Crosby biopsy capsule (11) and its modification as a pediatric biopsy capsule that made this diagnostic technique popular and practical. The early days of small intestinal biopsies in children were overshadowed by occurrences of bowel perforation and even death, until it was appreciated that the adult capsule should not be used on infants. A pediatric capsule had to have a porthole diameter of 2.5 mm, compared with the adult diameter of 5 mm, to avoid this mishap (Fig. 2) (12).

The ability to both diagnose celiac disease accurately by small intestinal biopsy and to treat it simply and effectively with a gluten-free diet led to these children being gathered together into specialty clinics. Access to small intestinal mucosa made another big contribution to the development of pediatric gastroenterology, enabling disaccharidases to be assayed from the tissue obtained by biopsy. Congenital malabsorption of lactose in two siblings was described in 1959 by Holzel *et al.* (13) in Manchester, UK, but no enzyme assays of mucosal tissue was then possible. However, the small intestinal biopsy permitted disaccharidase assays to enable a classification of sugar malabsorption disorders (14, 15). Biochemists, including Dahlquist, Semenza, and Messer, contributed significantly to this development. It soon became clear that secondary disaccharidase deficiencies, especially following gastroen-

Table 1. *Medical events leading to the emergence of pediatric gastroenterology*

Small intestinal biopsy
Parenteral nutrition
Safe pediatric ileocolonoscopy
Percutaneous liver biopsy
Pathophysiology of hereditary disorders of absorption
Rise of gut immunology and food allergy
Oral rehydration
Improvement in pediatric surgery
Portoenterostomy (Kasai) procedure for biliary atresia
Organ transplantation
–Liver
–Small bowel
Pathophysiology of metabolic liver disease (*e.g.*, α1-antitrypsin genetic defect)
Genetic basis for disease
–Cystic fibrosis
–α1-antitrypsin disease
–Crohn disease



CŒLIAC DISEASE WITH ATROPHY OF THE SMALL-INTESTINE MUCOSA

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From: The Lancet, Nov. 2, 1957, pp. 876-877

Figure 1. The cover page of the classic article by Sakula J and Shiner M published in *Lancet* in 1957. This was the first report of an intestinal biopsy in a child, age 7, with celiac disease. [Reproduced with permission by (9).]

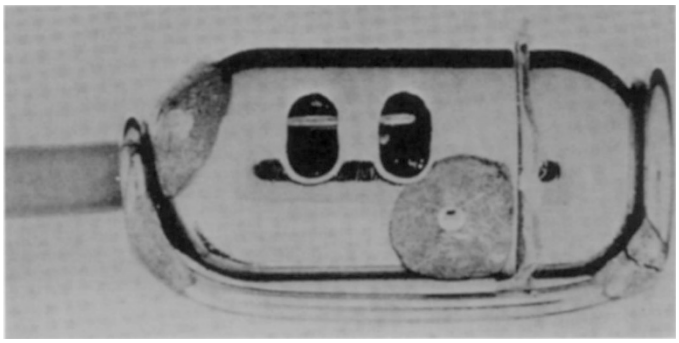


Figure 2. Photograph of a double-port small intestinal biopsy capsule. [Reproduced with permission from *Diseases of the Small Intestine in Childhood*, 4th Ed. Walker-Smith and Murch (eds) ISIS Medical Media, London, 1999, p 96.]

teritis, were common and important problems. Sunshine and Kretchmer (16) in Palo Alto, CA (Stanford University), and Burke and Anderson (17) in Melbourne, Australia, were the chief pioneers in this observation.

Obtaining direct access to small intestinal mucosa tissue was a remarkable achievement and led to a wealth of knowledge being obtained, particularly from the perspective of the effect of small intestinal disorders upon growth and development as well as upon disease states *per se*. Yet some pediatricians were opposed at first to the technique of small intestinal biopsy, as it was perceived to be too invasive for routine diagnostic use. Therefore, the use of noninvasive testing, such as breath hydrogen testing for carbohydrate malabsorption, was used as a less invasive way to make the diagnosis of lactase deficiency, etc.

The development of the technique of total parenteral nutrition by Wilmore and Dudrick (18) in 1968 was pivotal in development of this specialty as well as pediatric nutrition. Children with intractable diarrhea and other disorders who previously had been dying of starvation now had a chance to survive. This technique presented research opportunities. A series of disorders such as familial enteropathy (19), microvillous atrophy (20), tufting enteropathy (21), and autoimmune enteropathy (22) were recognized and treated by total parenteral nutrition. Later, successful small intestinal transplantation in children, developed in Pittsburgh, PA, Paris, France, and Omaha, NE (23), was used as a definitive treatment.

Recognition of the vital role of the immunologic function of the intestinal mucosa and its immaturity in young infants contributing to the pathogenesis of gastrointestinal disease states was pioneered by Allan Walker in Boston with his work on antigen entry (24). The existence of cow's milk sensitive enteropathy was established by serial small intestinal biopsies in Finland by Kuitunen and Savilahti (25). Subsequently, there has been recognition of the importance of disturbed immunologic function not only in gastrointestinal food allergy but in chronic inflammatory bowel disease as well. These disorders, particularly Crohn's disease, have become increasingly important in developed countries and play an ever-expanding role in pediatric gastroenterology practice. Studies of the pathogenesis of Crohn's disease and its management in children have received prominent attention at pediatric gastroenterology meetings in the last decade, as the field of mucosal immunology has expanded enormously.

In the developing world, with a decline in mortality from acute infectious diarrhea and with the advent of oral rehydration therapy, the problem of children with chronic or persistent diarrhea following acute diarrhea has emerged as an important therapeutic dilemma. Pediatric gastroenterologists such as Ulysses Fagundes Neto in Brazil have explored the relationship between infection, small intestinal mucosal damage, and food intolerance (26).

With increasingly sophisticated cell and molecular biology techniques, recognition of the pathophysiological basis of many gastrointestinal disorders in childhood was a major impetus to pediatric gastroenterological research. The principal hereditary disorders affecting digestion and absorption of fat, carbohydrate, and protein have been described. More recently, their genetic basis has been recognized using the techniques of molecular genetics and biology. Disorders first described in the 1960s are now understood on a genetic basis. This approach adds an important role for the pediatric gastroenterologist with a basic science background in the care of these patients.

Endoscopy combined with endoscopic biopsy has been a cornerstone for accurate diagnosis and now occupies a central place in pediatric gastroenterology. This has been a major factor in development of the specialty. More recently, pediatric upper and lower endoscopy has been widely practiced (27, 28). Indeed, upper endoscopy has replaced the Crosby capsule for small intestinal biopsy in most centers. More complex imaging techniques have become commonplace. This expansion of endoscopy has changed many units, as sometimes this technique dominates the work load. The improved technology specifically geared to children has led to emphasis by certain pediatric gastroenterologists on invasive endoscopy (endoscopic retrograde cholangiopancreatoscopy, percutaneous endoscopic gastrostomy, etc.) as a special interest within the field.

As enteral feeding for gastroenterological disorders became more sophisticated, gastroenterological dietetic skills and new therapeutic formulae assumed a more important role in pediatric gastroenterology practice. These advances in parenteral and enteral nutrition have helped the development of nutrition as a special interest within the field. The concept of the multidisciplinary team as the ideal care model for children with gastrointestinal disease has emerged from these innovations. This therapeutic approach is particularly useful in the management of newly diagnosed patients with Crohn's disease, particularly in the United Kingdom.

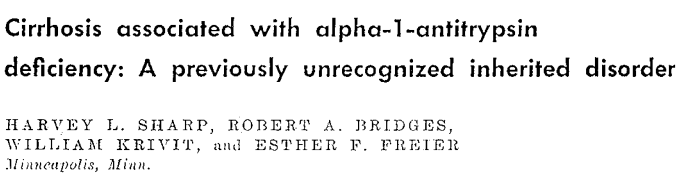
A major breakthrough in establishing the genetic basis for cystic fibrosis and the genotype/phenotype association has provided a more recent impetus for pediatric gastroenterology (29). The Human Genome Project, with further potential genetic breakthroughs for the molecular basis of disease, *e.g.* for Crohn's disease (30, 31), adds further support for ongoing research in identifying and treating pediatric gastrointestinal disease.

The recognition that liver disease in the pediatric population differed from that seen in adults, particularly the demonstration

of inborn errors in bilirubin and bile metabolism and of metabolic liver disease, was a strong stimulus to the development of pediatric hepatology within pediatric gastroenterology. Investigations focused on cholestasis of infancy to simplify the diagnostic dilemma, yet expanded the diagnostic possibilities beyond extra- and intrahepatic biliary atresia, choledochal cyst, and neonatal hepatitis. To do this, liver tissue was needed. The percutaneous liver biopsy was popularized and determined to be safe in infants and children without generalized anesthesia and did not require a cooperative patient. The technique of Hong and Schubert (32) was performed in 166 patients ranging in age from 1 wk to 15 y by Walker and Sharp in 1967 (33). They demonstrated that the diagnosis could be established by needle biopsy specimens for light and electron microscopy and that more than one "pass" could be performed to obtain biochemic determinations for accurate diagnosis by substrate and enzyme analysis. In Cincinnati, Hug, Shubert, and coworkers defined the various types of glycogen storage disease using this technique to it fullest capacity. Percutaneous liver biopsy was extremely accurate in predicting biliary atresia and, together with demonstrating bile flow or nonflow into the duodenum, essentially was 100% correct before laparotomy in determining which infants should undergo a portoenterostomy. During infancy, the liver pathology that most closely simulates extrahepatic biliary atresia is the liver disease associated with α-1-antitrypsin (α-1AT) deficiency, formerly one of the inherited forms of neonatal hepatitis. Not only was this association first reported by Sharp *et al.* (34) (Fig. 3), but Sharp used histologic techniques to document that the low levels of α-1AT resulted from its retention in the endoplasm's reticulum (ER) of the liver (35). It was the first of numerous genetic disorders that resulted in an improperly folded protein not secreted properly to the cell membrane or into the circulating blood. The PiZZ α-1AT actually aggregates in the ER, potentially leading to cell damage and cirrhosis. α-1AT deficiency is the most common inherited liver disease, presently requiring liver transplantation for cure. However, subsequent screening studies by Sveger and Eriksson (36) indicated that, even during infancy, $<$20% demonstrated any clinical evidence of liver disease and only a small percentage developed cirrhosis.

Bile acids were a focus of investigation in children because of pruritus, the potential for hepatobiliary toxicity, and the possibility of inborn errors in metabolism. Bile acids were thought to cause pruritus because of the observations that relief occurred by external bile draining, and its response to cholestyramine and/or phenobarbital in patients with a paucity of the intrahepatic bile ducts (Alagille syndrome). Secondary bile acids were documented in meconium using mass spectrometry by Sharp and Carey (37). Watkins and Lester documented bile acid deficiency in infants (38). Pure bile acids synthetic defects were to be defined later, after pediatric hepatology was further established (39).

With the recognition of these unique pediatric liver disorders and as organ transplant became more successful, major pediatric gastrointestinal programs included pediatric hepatologists or pediatric centers became dedicated to hepatic disease (Paris, London, Cincinnati, New York).


Cirrhosis associated with alpha-1-antitrypsin deficiency: A previously unrecognized inherited disorder

HARVEY L. SHARP, ROBERT A. BRIDGES, WILLIAM KRIVIT, and ESTHER F. FREIER
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From: J. Lab. & Clin. Med., 1969, 73(6):934-939.

Figure 3. The cover page of the classic article by Harvey Sharp *et al.*, published in the *Journal of Laboratory and Clinical Medicine* in 1969. This was the first report of α-1-antitrypsin deficiency associated with neonatal metabolic hepatitis. (Reproduced with permission by (34).]

FIRST CENTERS OF PEDIATRIC GASTROENTEROLOGY

Although fundamental advances in knowledge of diseases such as celiac disease and cystic fibrosis occurred during the late 19th and early 20th centuries, it was not until the early 1960s that centers for gastroenterological disorders in children began to emerge in North America, Great Britain, Australia, and the continent of Europe. Table 2 outlines these events.

Dolf Weijers, working in Utrecht in the Netherlands with the biochemist, van de Kamer, and initially with Dicke, developed one of the first centers for pediatric gastroenterology. Key to this successful development was the collaboration between pediatricians and biochemists who could carry out estimations of fecal fat in celiac patients on and off gluten.

Charlotte Anderson at the Royal Children's Hospital in Melbourne in the early 1960s developed a clinical and research program in pediatric gastroenterology and established a Gastroenterological Research Unit. She carried forward the observation of the benefits of a gluten-free diet in celiac patients during a research fellowship (1951–1953) in Birmingham, England, with Alistair Frazer using biochemical observations. Her most important contribution was to clearly establish the need for a specialized expertise in gastroenterology in children. Her book, *Pediatric Gastroenterology*, which she co-edited with Valerie Burke in 1975 (40) (one of the first texts in

Table 2. *Milestones in the establishment of pediatric gastroenterology*

1968	European Society of Pediatric Gastroenterology and Nutrition (ESGPAN) holds first annual meeting in Paris
1969	"Pediatric Gut Club" formed
1973	North American Society for Pediatric Gastroenterology and Nutrition (NASPGN) founded
1978	First ESPGAN/NASPGN Joint Meeting held, Paris, France
1984	First Annual Meeting of NASPGN held, Chicago
1990	First pediatric gastrointestinal subspecialty board created in United States
1990	*Journal of Pediatric Gastroenterology and Nutrition*, the Official Journal of ESPGHAN/NASPGHAN, begins publication
2000	First World Congress of Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN, NASPGHAN, APPSPGN, and LASPGN) held

ESPGHAN, European Society for Pediatric Gastroenterology, Hepatology and Nutrition; NASPGHAN, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; APPSPGN, Asian Panpacific Society for Pediatric Gastroenterology and Nutrition; LASPGN, Latin American Society for Pediatric Gastroenterology and Nutrition.

pediatric gastroenterology), played an important role in this development. Her work chiefly centered on celiac disease, cystic fibrosis, and sugar intolerance, but, above all, her personal experience centered upon problems related to the small intestine. She was the first to show that the small bowel mucosa could heal on a gluten-free diet (41). She also developed a simple, noninvasive diagnostic test to detect excess stool-reducing substances, which has proved to be of practical value for the diagnosis of sugar intolerance in infants (42).

The same Melbourne center was later the location of the first recognition of rotavirus by the virologist Ruth Bishop, working with her clinical colleagues at the Royal Children's Hospital (43). Birmingham also continued to be an important center for gut and liver disease. More recently, it has become an important center for small intestinal and liver transplantation.

From the outset of this field, Paris has played a key role, with Jean Rey emphasizing the importance of clinical nutrition. Jacques Schmitz developed a major interest in the small intestine, focusing at first upon congenital disorders of absorption. Claude Ricour and Olivier Goulet, with others, developed parenteral nutrition (including home parenteral nutrition) and, with doctors in research centers (Omaha and Pittsburgh), were pioneers in small intestinal transplantation in children.

In Lund, Sweden, Bertil Linquist developed an important center with a special interest in nutrition and gut pathophysiology. Glucose-galactose malabsorption was first reported there (44). London was an important center for the development of pediatric gastroenterology, with the first two chairs of pediatric gastroenterology held by John Harries and John Walker-Smith, followed more recently by Ian Sanderson and Peter Milla. These workers focused upon luminal gastroenterology, with a special interest in diseases of the intestine.

Pediatric hepatology in Europe began in Paris at Bicetre Hospital in 1964 when Professor Alagille was appointed as Head of the Pediatric Service. The unit rapidly became internationally renowned for their early work in pediatric hepatology. Working with Professor Odievre, Professor Alagille wrote a book, *Maladies du foie et des voies biliaires chez l'enfant*, published in French in 1978 and in English in 1979. Professor Alagille developed a multidisciplinary group including many famous hepatobiliary surgeons, Professor H. Bismuth and Professor J. Valayer. The first liver transplant in Paris was performed in 1981 by Professor Bismuth at Bicetre Hospital. The work of the unit continues under the guidance of Professor Olivier Bernard and Dr. Michele Hadchouel, who have made particular contributions in the genetics of liver disease in children. In Britain, the first center for pediatric hepatology was developed at King's College Hospital in London in 1970, when Dr. Alex Mowat was appointed as a pediatrician with a special interest in hepatology and gastroenterology. He was joined by Professor Ted Howard, who had a particular interest in the Kasai portoenterostomy for biliary atresia and was considered a world expert in the management of this disease. The publication of Mowat's first book, *Liver Disorder in Childhood*, in 1979 (45) indicated that pediatric hepatology had now become distinct from adult hepatology. In 1989, a second national liver unit was developed at Birmingham under the guidance of Deirdre Kelly, and her unit pioneered pediatric liver transplantation in the United Kingdom, introducing reduction hepatectomies in 1989 and split liver grafting in 1993. The unit subsequently developed small bowel and liver transplantation in 1997 and is the only unit to do so in the United Kingdom. Alex Mowat held the first chair of pediatric hepatology in the United Kingdom, followed by Giorgina Mieli-Vergani, both at the University of London, and subsequently Deirdre Kelly, University of Birmingham.

The University of London has played a major role in the academic recognition of pediatric gastroenterology (including hepatology) by making a number of appointments from the early 1970s onward. These included a chair in gut immunology for Tom Macdonald, a scientist whose research in immunology has focused upon gastroenterological disease in children and the use of the fetal intestinal organ culture model.

Finland has been a significant force in pediatric gastroenterology, with centers in Helsinki and, later, Tampere, lead by Jarmo Visakorpi. The principal focus at first was upon celiac disease, continuing today with Markku Maki, as well as upon gastroenteritis and food allergy.

Switzerland, too, played an important role at the beginning of the specialty. Zurich was an early center for pediatric gastroenterology, fostered by Andrea Prader with his interest in child growth and development. There, David Shmerling performed early studies of gluten elimination and challenge in celiac disease. Salvatore Auricchio and the biochemist Giorgio Semenza were pioneers in understanding disorders of sugar absorption. In Berne, Ettore Rossi founded an important center where trainees Beat Hadorn and Michael Lentze subsequently developed major research studies of the pathophysiology of absorption. They later founded important German centers in Munich and Bonn, respectively.

After his training in Zurich, Salvatore Auricchio developed a major center in Naples, where a sister unit was developed and directed by Amido Rubino. Naples has played a major role in research on celiac disease and the physiology of absorption, including studies related to oral rehydration therapy, with the work of Stefano Guandalini and Alessio Fasano. An important center developed in Brussels lead by E. Eggermont and Helmuth Loeb, with Samy Cadranel being a pioneer in endoscopy for children.

In North America, several centers of excellence developed at about the same time. Murray Davidson at Albert Einstein Medical School and the Bronx Lebanon Hospital in New York established a pediatric gastroenterology program directed at inflammatory bowel disease, infectious diarrhea, and motility disorders associated with gastrointestinal problems such as constipation and gastroesophageal reflux. Davidson developed an interest in pediatric gastroenterology as a pediatric resident at Cornell in the 1950s and was trained at the same institution by the adult gastroenterologist Tom Almy. An award for excellence in Pediatric Gastroenterology and Nutrition by the GI/Nutrition Section of the American Academy of Pediatrics is given annually to commemorate his contribution to the field. Davidson, in collaboration with his trainees, Claude Morin (the first Director of Pediatric Gastroenterology at St. Justine's Hospital at the University of Montreal) (46), and later with Mervin Silverberg (Chairman of Pediatrics at North Shore

Hospital, an affiliate of Cornell University School of Medicine) (47), published the first two reviews of gastrointestinal disease in pediatric patients. Albert Einstein Medical School also contributed to the development of pediatric hepatology in that Alex Mowat, who went on to found the world-renowned liver center at King's College in London, trained there with the adult hepatologist Irwin Arias.

In Boston, Harry Shwachman established a center of excellence for pediatric gastroenterology in the late 1950s and early 1960s. His interest in cystic fibrosis provided many observations on the gastrointestinal manifestations of this condition. Dr. Shwachman, through a refinement in the intestinal biopsy capsule to obtain small intestinal mucosal tissue, helped to define disaccharidase deficiencies and other lesions of small intestinal mucosa with Irena Antonowicz and Emi Lebenthal. This center eventually developed into a major training program for pediatric gastroenterologists under Richard Grand (1972–1982) and Allan Walker (1982–2001) (both Grand and Walker trained initially with Dr. Kurt Isselbacher in adult gastroenterology at Massachusetts General Hospital). To commemorate Dr. Shwachman's contributions to the field, the Shwachman Award was established in 1984 by the North American Society for Pediatric Gastroenterology and Nutrition, to be given annually to an individual recognized for excellence in the field (Table 3).

Gastroenterology and hepatology developed independent of nutrition at the Hospital for Sick Children (HSC) in Toronto, Ontario, Canada. It was initially led by Andrew Sass-Kortsak, a biochemist who helped identify many inborn errors in liver function, and continued under Dick Hamilton, who trained in adult gastroenterology and studied intestinal transport with Jack French at the Queen Elizabeth Hospital in Birmingham. Hamilton, with Gordon Forstner, Grant Gall, and others, went on to develop one of the premiere training programs in pediatric gastroenterology in the world at HSC. Many leaders of Australian pediatric gastroenterology programs today obtained their training with Dick Hamilton. In 1995, nutrition and pediatric gastroenterology at HSC were combined into a single program under the leadership of Peter Durie. HSC was also the institution where the defective CFTR gene causing cystic fibrosis was cloned (29).

Centers of excellence in pediatric hepatology have also developed in several North American medical centers during the same period as a result of the recognition of unique liver diseases in infants and children. The contributions of Andrew Sass-Kortsak at HSC have already been mentioned. In the same setting, Michael Thaler became interested in pediatric hepatic disease under the influence of Stanley Hartroft, an internationally recognized hepatic pathologist in Toronto. After a brief training period in Paris and at Tufts New England Medical Center, Thaler established a major training center in pediatric gastroenterology with an emphasis in hepatology at the University of California in San Francisco. In Minneapolis, at the University of Minnesota, Harvey Sharp established a strong pediatric gastrointestinal tradition with an emphasis on hepatology. Sharp's publication in 1967 (34) of α-1AT deficiency as a major cause of neonatal hepatitis was a seminal observation that helped define pediatric hepatology as a separate entity from adult hepatology (Fig. 3). Another major center of excellence in pediatric hepatology was at the Cincinnati Children's Hospital under Bill Balistreri, who had trained in pediatric gastroenterology at the Children's Hospital of Pennsylvania. The Cincinnati center in pediatric hepatology has produced major leaders in the field, such as Fred Suchy, senior editor of a definitive textbook in hepatology and chairman of the Department of Pediatrics at Mt. Sinai Medical School in New York, and Ron Sokol, University of Colorado in Denver. Claude Roy, after training with Arnold Silverman in Denver, also established a strong program in hepatology at Sainte Justine Hospital in Montreal. At the same time, John Watkins established a major center in neonatal hepatic disorders as part of his pediatric gastroenterology training program at the Children's Hospital of Philadelphia. Marvin Ament, after training in adult gastroenterology with Cy Rubin at the University of Washington, developed a major clinical training program in pediatric gastroenterology, with a strong emphasis on nutrition at the University of California in Los Angeles. Marvin Ament's trainees have gone on to head major programs elsewhere, including Jon Vanderhoof in Omaha. The Omaha program today is a major center for liver and bowel transplantation. Peter Whitington, who trained with Jerry Odell at the University of Wisconsin, developed a strong program in pediatric hepatology, initially at the University of Chicago and currently at the Children's Memorial Hospital in Chicago. His program has a strong emphasis on liver transplantation and was the first pediatric hepatology center to introduce a living donor option.

Many other important centers of pediatric gastroenterology and nutrition have developed, including those in Sydney, Adelaide, Brisbane, Jerusalem, Sao Paolo, Santiago, Taipei, and Tokyo. In this brief review it is not possible to mention all such centers. Our focus has been on those that had the greatest international impact, both by the quality of their clinical and research work and by the influence they had across the world by training young people.

Table 3. *Recipients of the Harry Shwachman Award*

1987	Claude C. Roy, MD
1988	Arnold Silverman, MD
1989	Murray Davidson, MD
1990	J. Richard Hamilton, MD
1991	Otakar Koldovsky, MD, PhD
1992	Samuel Foman, MD
1993	Richard J. Grand, MD
1994	Gerard B. Odell, MD
1995	W. Allan Walker, MD
1996	Joyce Gryboski, MD
1997	John B. Watkins, MD
1998	Marvin Ament, MD
1999	William Balistreri, MD
2000	William Klish, MD
2001	Jon Vanderhoof, MD

PEDIATRIC GASTROENTEROLOGY SOCIETIES

The European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN). It was in November 1967 that Dolf Weijers took the initiative to invite to Utrecht

Bertil Lindquist of Sweden and Jean Rey of France to discuss plans to set up a society for pediatricians whose main discipline was pediatric gastroenterology. They were joined by Jan van de Kamer, the distinguished biochemist (48).

This led to the foundation of the European Society for Pediatric Gastroenterology (ESPG), which held its first meeting in Paris in 1968. The first council consisted of Dolf Weijers (Utrecht, the Netherlands) as president, Bertil Lindquist (Lund, Sweden) as secretary, and Jean Rey, (Paris, France), Charlotte Anderson (Birmingham, U.K.), and Salvatore Auricchio (Naples, Italy) as council members. The aim was to create a forum for presentation and discussion of the research activities being pursued in pediatric gastroenterology throughout Europe. In 1976 at the Weimar meeting, nutrition was added to the title of the society, which now had the acronym ESPGAN. From the beginning, the important interrelationship between clinical nutrition and gastroenterology was appreciated and the society's committee of nutrition published several influential guidelines as supplements to *Acta Pediatrica Scandinavia*.

It is noteworthy that this was the first society of pediatric gastroenterology in the world. Unlike adult gastroenterology, international societies emerged several years before national bodies, *e.g.* the British Society was only founded in 1986, although a more informal British Pediatric Gastroenterology Group had existed from 1974. In 1990, the European society made the decision to add hepatology to the title, *i.e.* European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), to give due recognition to the vitally important group of liver disorders in children and to avoid a split within the society.

In Paris in 1978, the society met for the first time in a joint meeting with the North American Society for Pediatric Gastroenterology and Nutrition (NASPGN) and then every 4 y thereafter. At the second meeting of ESPG in Interlaken, Switzerland, the first workshop on celiac disease was held when the modern diagnostic criteria for celiac disease were first laid down based upon elimination and challenge with gluten, related to serial small intestinal biopsies (49). Since then, the Interlaken or ESPG (later ESPGAN) diagnostic criteria have had a notable influence in further understanding of celiac disease and cultivating research in this field. Over the years, the ESPGAN criteria have been refined and, in 1990, revised (50). In addition, a multicenter study of the epidemiology of celiac disease proved to be of great importance.

This successful diagnostic workshop led to the concept of working groups sponsored by ESPGHAN in a number of areas within pediatric gastroenterology, which have been very productive over a number of years. Some have lead to recommendations in other areas, for example, the composition of oral rehydration solutions (ORS). In fact, oral rehydration therapy, one of the most effective tools available to the practicing pediatric gastroenterologist, was developed by a group of epidemiologists and adult specialists, largely from the United States (51), working in the developing world who were particularly interested in adult cholera at first (52). Their interests, however, extended to noncholera diarrhea as well and to children also. In the 1970s, acute infectious diarrhea was killing millions of children in the developing world each year. The introduction of ORS led to a significant reduction in infant and child mortality in the developing world. Based chiefly upon research lead by Michael Farthing (53), the ESPGHAN working group recommended a modification in the composition of ORS for the children of Europe (52), *e.g.* a developed community, to a low-sodium, low-osmolality solution. A recent meta-analysis of children (chiefly from developing communities) admitted to a hospital with diarrhea-associated dehydration found reduced osmolarity rehydration solution, when compared with standard World Health Organization rehydration solution, lowered the need for intravenous infusions, lowered stool volume, and caused less vomiting (54). However, this conclusion is contentious in other settings (55).

The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). A special interest in gastrointestinal diseases in infants and children dates back to the early 1960s, when Norman Kretchmer, then president of the Society for Pediatric Research, established at its annual meeting a gastrointestinal subsection for platform presentations chaired by Joyce Gryboski. The key academicians providing the impetus for this new area of interest were Murray Davidson (New York) and Harry Shwachman (Boston), Gulio Barbaro (Columbus, MO), and Frank Cozzetto (Denver). Barbaro had a major interest in functional disorders of the intestine and Cozzetto in metabolic/biochemical diseases. In addition, pediatricians interested in liver disease met in Chicago in a setting that was more like a small "liver club" and had extensive discussions about research on liver diseases in children. At this time, a limited number of hepatologists and pathologists would come to Chicago to present abstracts and discuss research. The Chicago meetings grew into the larger and more formal American Association for the Study of Liver Disease (AASLD). Eventually, the pediatric hepatology discussions, in conjunction with the gastrointestinal section at the Society of Pediatric Research, resulted in the formation in 1969 of the "Pediatric Gut Club" and an evening symposia on pediatric GI topics at the APS-SPR meetings. These parallel interactions among gastroenterologists and hepatologists were eventually formalized when Merv Silverberg (Albert Einstein Medical School) and Dan Caplan (Emory Medical School) proposed that the North American Society for Pediatric Gastroenterology be established in 1973, with Silverberg as its first president and Caplan as secretary/treasurer. The venue for this newly established society moved from the Society for Pediatric Research meeting to the annual American Gastroenterology Association meeting, where a separate pediatric gastroenterology symposium and business meeting was held as a satellite meeting within the larger adult gastroenterology society meeting. In 1984, NASPGN established its own annual meeting in Chicago, which has been held every year since either separately or in conjunction with the ESPGHAN. As with the European experience, the founders of pediatric gastroenterology trained first in adult gastroenterology after a pediatric residency and then adapted their experience and techniques to the care of children with gastrointestinal problems. As mentioned, the first major publication outlining gastrointestinal conditions unique to Pediatrics was authored by Morin and Davidson as a review in *Gastroenterology* in 1967 (46) and was followed closely by

another review in *Gastroenterology* by Silverberg and Davidson in 1970 (47). These comprehensive reviews published in a predominately adult disease-oriented gastroenterology journal underscored the importance of establishing a subspecialty in gastroenterology for pediatrics.

As with ESPGAN, the NASPGN established standing committees on clinical care, research, and nutrition, published clinical policies and training standards, and, more recently, established a foundation to support young investigators in the field and to encourage pediatric residents to consider gastroenterology as a subspecialty. Very recently, hepatology was added to the society's name, which is now NASPGHAN.

Other international societies and the Federation of Societies of Pediatric Gastroenterology and Nutrition. The Latin American Society for Pediatric Gastroenterology and Nutrition (LAPSGAN) was founded in October 1974 in Buenos Aires. There were four founders, Horacio Toccalini (the pioneer of pediatric gastroenterology in Latin America) and Ricardo Licastro from Argentina and Jose Vicente Martins Campos and Ulysses Fagundes-Neto from Brazil. Their goal was to model the society after ESPGHAN and to encourage young doctors to develop the field and especially an understanding and management of diarrhea and malnutrition in children, a major regional problem.

The Asian Pan Pacific Society of Pediatric Gastroenterology (APPSPGN) was founded in Tokyo in 1993 with Geoff Cleghorn (Brisbane) as first president followed by Yuichiro Yamashiro (Tokyo). APPSPGN grew out of an earlier body formed in the 1960s by Michael Gracey of Australia with several Indonesian colleagues (Sunoto and Agus Firmansaya). Regular regional conferences and teaching workshops are held every other year.

Finally, the Commonwealth Association of Pediatric Gastroenterology and Nutrition (CAPGAN) was founded in 1994 in Hong Kong, with a focus on interaction between developing and developed communities. It had evolved from Commonwealth Conferences on Diarrhea and Malnutrition in Childhood held from 1983 in London, New Delhi, Hong Kong, Karachi, and Darwin. In recent times, it has had a particular focus on AIDS in childhood.

Finally, in 2000, following upon the first world congress of pediatric gastroenterology and nutrition in Boston, the Federation of Societies of Pediatric Gastroenterology, Hepatology and Nutrition (FSPGHAN) was established to coalesce pediatric gastroenterology as a world body, with Stefano Guandalini as its first president.

Formal qualifications—board examinations. In the United States, committees to determine guidelines for training in pediatric gastroenterology were developed in the 1980s, which lead to the establishment of subspecialty boards in pediatric gastroenterology given for the first time in 1990 under the aegis of the American Board of Pediatrics and its Pediatric Gastroenterology and Nutrition subspecialty subboard chaired by Bill Klish (Houston). Since then, the boards, given every other year, have certified more than 600 pediatricians. As a result of subspecialty boards, the Residency Review Committee for Pediatrics, a subsidiary of the Accreditation Council on Graduate Medical Education (ACGME), has also certified over 35 training centers in this subspecialty in the United States. These centers must be recertified every 4 y.

In 1997, the subspecialty advisory committee for pediatric gastroenterology of the Royal College of Pediatrics and Child Health in Great Britain established a formal training program for pediatric gastroenterology and approved centers for training. For a pediatrician to be licensed as a pediatric gastroenterologist, he must have a relevant certificate that he has successfully had such a formal training period. A detailed syllabus and training requirements have been developed largely based upon American training programs. In Canada, there has been a formal written and oral examination for at least a decade, as well as training requirements and suitability of subspecialty training programs, all supervised by the Royal College of Physicians and Surgeons. Europe is now beginning to examine the issue of training in pediatric gastroenterology within the European Union.

INTERNATIONAL CONFERENCES

Since the late 1960s, regular international conferences concerning pediatric gastroenterology have been held, beginning in Europe and North America and extending internationally, culminating in a World Congress for the four major pediatric gastroenterology societies in Boston in 2000. These conferences have been an important catalyst for the development of a discipline where, at first, the number of practitioners in most countries was small. This interaction with like-minded colleagues was vital to the development of the discipline. Throughout, a strong scientific basis has been a feature of these conferences, as pediatric gastroenterology is firmly rooted in clinical science and many scientists have contributed to the meetings. ESPGHAN and NASPGHN have always prided themselves on the inclusion of scientists among their members. Pediatric gastroenterologists have also continued to contribute to adult meetings such as Digestive Disease Week and the United European Gastroenterology Week as well as the adult world gastroenterology congresses. In this way, vital insights are shared.

ROLE OF TEXTBOOKS

The first textbook in this discipline was published in 1971 with Arnold Silverman, Claude Roy, and Frank Cozzetto as co-authors (56), all from the Pediatric Gastroenterology Center in Denver. A subsequent edition was published by Roy in Montreal. In their preface, the authors describe, as mentioned, the increased momentum for the recognition of pediatric gastroenterology following the publication in *Gastroenterology* of the reviews of major pediatric gastroenterology disease states first in 1967 (46) and then in 1970 (47). This North American publication emphasized structural abnormalities of the gastrointestinal tract and, among other things, the importance of chronic inflammatory bowel disease. In 1975, Anderson and Burke published a text emphasizing celiac disease (40). In the same year, a similar emphasis also occurred in the text entitled *Diseases of the Small Intestine in Childhood* (57). Also in 1975, Gryboski (58) wrote a text describing the gastrointestinal problems confined to infancy. These were the first four texts in

the English language. They signaled the arrival of pediatric gastroenterology as a legitimate pediatric subspecialty.

In 1991 a large, two-volume, multiple-authored text appeared, edited by Walker and colleagues (59). By then it was clear that the specialty had come of age and disciplines such as pediatric hepatology were fully developed within the field. This comprehensive textbook, entitled *Pediatric Gastrointestinal Disease: Pathophysiology, Diagnosis, Treatment*, was designed as a resource for health care professionals dealing with children with gastrointestinal and nutritional problems. Sections on development, pathophysiology, diagnosis and treatment provided an in-depth discussion of common and uncommon pediatric problems. In the opening chapter, Dick Hamilton (60) stated that "pediatric gastroenterology has come of age" and pointed out that in pediatrics a thorough understanding of normal development and the maturation of the digestive system is essential before pediatric gastroenterologists can deal with sick children.

ROLE OF THE *JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION*

The role of medical publications as disseminators of new discoveries goes back as far as the 17th century Philosophical Transactions. In the 18th century, the concept arose that a medical journal should not only report on empirical research but just as importantly report upon criticism. Since the 18th century, there has been a steady progression of new specialist journals as each branch of medicine has emerged, beginning with broad tracts of knowledge such as physiology to ever smaller clinically based disciplines such as gastroenterology. In Germany, the first gastroenterological journal, *Archiv fur Verdaungskrankeiten*, was published in 1895. More recently, pediatric specialty journals have emerged. The *Journal of Pediatric Gastroenterology and Nutrition* (JPGN) was first published in 1982, with Emi Lebenthal as the first editor-in-chief and Ettore Rossi as its associate editor. In 1991, JPGN became the official journal of both ESPGHAN and NASPGHN, with Bill Balistreri and Michael Lentze as the first editors-in-chief. This journal has played an important role in consolidating the development of pediatric gastroenterology and providing evidence for the legitimacy of this specialty. It has also played a role as an international newspaper for the specialty. In its first editorial, the close collaboration of basic and clinical research was emphasized as an important feature of pediatric gastroenterology. The JPGN has given great emphasis to the clinical science base of this specialty throughout its 20 y of publication. Recently, APPSPGN and LASPGN have become affiliated with the journal. The journal thus represents the worldwide field of pediatric gastroenterology.

CONCLUSION

Hamilton (60) has described "a pediatric specialty as having professional status once it has a peer-reviewed journal, professional associations, task forces (in Europe working groups) and examinations to assess professional competence." We have endeavored in this brief review to indicate how these arose internationally, although examinations for pediatric gastroenterology are at present confined to the United States and Canada. This specialty is only 40–50 y old. A great deal has been achieved, but so much remains to be done for sick children with gastrointestinal disease, both in treatment and prevention, and with a particular challenge in the developing world. It is the interaction with the developing world that at present offers the greatest opportunity for the future.

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