DDICC Meeting Minutes
December 11, 2001

Digestive Diseases Interagency Coordinating Committee (DDICC)

Meeting Topic: Pediatric Gastroenterology, Hepatology, and Nutrition

Meeting Location: National Institutes of Health
Building 31C, 6th Floor, Room 7
Bethesda, MD

Chair:	**Organization**
Jay Hoofnagle, M.D.	NIDDK

Participants:

Mitchell Cohen, MD	NASPGHAN
Richard Colletti, MD	NASPGHAN
James Everhart	NIDDK
George Ferry, MD	CDHNF
Lisa Ganshereff	NIDDK
Frank Hamilton, MD, MPH	NIDDK
Brian Harvey, MD, PhD	FDA
Jay Hoofnagle, MD	NIDDK
Van Hubbard, MD	NIDDK
Stephen James, MD	NIDDK
M. Khan	CSR
Catherine Loria	NHLBI
Anita Moncrease	HRSA
Judy Podskalny	NIDDK
Sharon Pope	OSPPA-NIDDK
Patricia Robuck, PhD, MPH	NIDDK
Allen Spiegel, MD	NIDDK
Hugo Gallo Torres, MD	FDA
Karen Winer	NICHD
Harland S. Winter, MD	NASPGHAN

Research Agenda:

Richard Grand, MD	NASPGHAN/CDHNF
Philip Sherman, MD	NASPGHAN/CDHNF

A complete list of the DDICC members is attached as Appendix 1.
A list of acronyms is attached as Appendix 2.

Welcome and Introductions

Jay H. Hoofnagle, M.D., Director of the Division of Digestive Diseases and Nutrition at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and Chair of the Digestive Diseases Interagency Coordinating Committee (DDICC), welcomed participants and explained the purpose of the DDICC. As an interagency coordinating committee mandated by the U.S. Congress, the DDICC meets four times a year to discuss areas of collaboration among the various NIH Institutes and Centers (ICs) and other Federal agencies. In general, this forum is useful for discussing ideas for initiatives and meeting with the community to hear their concerns about research in digestive diseases. The purpose of this meeting was to hear presentations from the community of pediatric gastroenterologists on the suggested research agenda and ideas for initiatives.

Presentations

Dr. Cohen, NASPGHAN

Mitchell Cohen, M.D., of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN), provided a summary of NASPGHAN's goals. A major professional pediatric society, NASPGHAN is a vibrant organization with its own constituency. The Society was founded in 1973 and has grown to a membership of approximately 880 individuals throughout North America, approximately 75 percent of whom are affiliated with academia. At any given time, about 20 percent of NASPGHAN members are active in committee work. NASPGHAN is a representative group and it is a group of experts in the field with an important message to deliver. More than 40 NASPGHAN members were involved in creating the research agenda presented at this meeting.

The mission of NASPGHAN is to be a world leader in advancing the science and clinical practice of pediatric gastroenterology, hepatology, and nutrition. Pediatric gastroenterology research is important because the diseases are unique to childhood and because many digestive diseases that occur in adulthood begin in childhood. Addressing pediatric digestive diseases is important to achieving a healthy Nation. Beginning with this meeting, the Society's objective is to establish a partnership among NASPGHAN, the Children's Digestive Health and Nutrition Foundation (CDHNF), and the National Institutes of Health (NIH) to make pediatric gastroenterology research a top priority.

In order to present information about the importance of pediatric digestive diseases, Dr. Cohen summarized data from the pediatric health information system (PHIS) database, a database of 35 major pediatric hospitals in 20 States that is representative of pediatric health throughout the United States. Digestive diseases accounted for 52,000 inpatient visits, approximately 15 percent of the total pediatric admissions for this large group of children's hospitals (second only to respiratory illnesses). As a percentage of the total, digestive diseases comprises approximately 15 percent of inpatient visits, 13 percent of total inpatient days, and 11 percent of total inpatient dollars (11 percent of $7.31 billion) in this group of pediatric hospitals.

Regarding workforce issues, about 14 percent of pediatric gastroenterology time is spent in research, a relatively small number; 5 percent of pediatric gastroenterology time is spent in extramural funded research, 80 percent of which is funded by the NIH. Only 10 percent of pediatric gastroenterologists spend more than half their time in research, and only 3 percent spend more than three-quarters of their time in research. Despite NASPGHAN's organizational strengths and expertise and despite the need, there is a critical shortage of pediatric gastroenterology researchers. As part of the NASPGHAN effort to address this concern, the CDHNF was created.

Dr. Ferry, CDHNF

George Ferry, M.D., CDHNF, summarized his organization's mission and research emphasis. CDHNF was formed to concentrate on stimulating more research dollars and more and better-trained researchers. The Foundation's mission is to improve the educational activities of NASPGHAN that can extend beyond its physician members to the public.

Currently, CDHNF is funding 1 or 2 new investigator development awards per year. The Foundation has also been participating in an endoscopy outcomes research initiative for the past year. CDHNF is interested in stimulating cross-pollination of ideas and in fostering partnerships in research and education between NASPGHAN members and the U.S. Food and Drug Administration (FDA), industry, and the NIH, in the hopes of conducting workshops that lead to publications and ideas for future research. Although the CDHNF is attempting to identify and fund research on its own, the Foundation would like to partner with other entities to achieve maximum use of available research dollars.

The leadership of the CDHNF overlaps with that of the NASPGHAN. In addition to NASPGHAN members, the Foundation includes lay members from industry and business. During the past 5 years, the CDHNF has raised almost $700,000 to support research projects and the creation of the research agenda currently under discussion. One of the reasons the CDHNF funded this research agenda is to focus on research needs and how to foster partnerships with other groups to improve the number of researchers in this specialty.

Research Agenda Overview: Dr. Sherman

Philip Sherman, M.D., NASPGHAN/CDHNF, provided an overview of the research agenda. Dr. Sherman explained that he is one of the 3 percent of pediatric gastroenterologists who spend more than 75 percent of their time conducting research. The goal of research in this area is to improve the health and needs of a neglected portion of society – children with digestive disorders.

This research agenda was conceived by Harland Winter, past president of NASPGHAN, and his predecessor, Ron Sokol, a pediatric hepatologist in Denver, Colorado. Its purpose is to highlight areas of research that are critical for advancing the field and areas in which resources targeted to research can make a difference, over the next few years, to advance the field with practical implications. Each of the (more than 50) members who participated in creating this agenda were charged with the task of identifying the burden of illness: how common are these diseases, what

would be the impact of providing support in research, and a definition of the gaps in current knowledge. Although funding of basic research is important, the intent of this agenda was to focus and target the document to feasible of the proposals for research funding.

The research agenda is a work in progress, the result of input from individuals from across the United States and Canada – basic scientists, adult gastroenterologists as well as pediatric gastroenterologists, hepatologists, and pancreatologists. It is a work by consensus, so it does not represent any particular age group or constituency and it is a broad-based initiative across the discipline of pediatric gastroenterology.

In each of the areas outlined in this document, NASPGHAN would like to partner with the appropriate NIH Institute or Center to help advance the knowledge related to children affected with these disorders. Dr. Sherman provided a clinical example of a young girl with a rare and fatal condition. He emphasized that the way this girl metabolizes drugs is different than that of an adult. Understanding the pathophysiology of this rare disease will provide important information about many treatments for conditions that affect her rare condition as well as more common conditions affecting individuals of all ages.

[Electronic copies of the research agenda can be obtained by contacting Dr. Sherman.]

Research Agenda, by Chapter: Dr. Grand

On behalf of NASPGHAN and CDHNF, Dick Grand, M.D., thanked the NIH participants at this meeting. He presented overviews of some of the chapters in the research agenda. The committees that wrote the chapters were asked to use their imaginations to analyze the current state of pediatric digestive disease research and to report on possibilities for its future direction.

The research agenda begins with a discussion of the molecular basis of gastrointestinal disease, focusing on new opportunities for research. The Human Genome Project and proteomics have opened significant opportunities for research in pediatric digestive diseases that were not heretofore available. One of the main topics of focus – and a recurring theme throughout the research agenda – is to define the genetic basis of disease and to analyze genotype/phenotype correlations and modifiers.

Animal Models. Continuing to develop new animal models of human disease is an area in which much important information has already been developed. The background genetics of the animal influences the expression of disease; this is true in humans, but how it happens is not entirely clear. Modifier genes in the expression of human disease and the interaction of genes within humans are two new areas in which animal models are needed.

Preventive and Therapeutic Interventions. Novel preventive and therapeutic interventions need to be developed, with emphasis on cell transplantation and use of chimeric oligonucleotides. For example, in cystic fibrosis (CF), a simple substance – phenyl butyric acid – acts as a chemical chaperone and can take an aberrant CF cell and help to deliver the CFTR protein to the surface, even though by itself CFTR will not cross the cell onto the apical membrane. One example of such research is a study conducted by Warren Strober that used

oligonucleotides against NF-kappa-B to control experimental inflammatory bowel disease (IBD) by anti-sense NF-kappa-B.

Tools for Diagnostic and Population Screening. The significant challenge here is to find diagnostic and population screening tools that are highly sensitive and very specific.

Developmental Physiology and Pathophysiology. It is important to begin to look at both gene expression profiles in development and in disease to see how abnormal genes affect cell function. More information is needed about the physiologic impact of mutated genes, the role of growth factors in intestinal development and differentiation, the ability to stimulate gut growth, and the role of non-epithelial cell types in epithelial cell function (in development and in disease). Understanding the developmental growth factors may offer insight into how to treat patients with short bowel. Information about how cells talk to each other and their messages and messengers will be crucial.

Relationship of Nutrient Intake and Development. This area has not been tapped, especially with regard to the fact that the human fetus swallows large amounts of amniotic fluid. Amniotic fluid has been analyzed in various stages of gestation but the adaptive advantages of swallowing amniotic fluid are not known, including what protection and what stimulus to growth may be provided. Understanding how nutrients regulate gastrointestinal function and the function of the organism as a whole will also prove important.

Secretion and Diarrhea. Secretion and diarrhea is of importance because it encompasses infectious diarrhea, a major health problem worldwide including in the United States. The first goal is to define membrane and epithelial cell biology, focusing specifically on the interaction between bacteria and intestinal mechanisms. The second goal is to delineate mechanisms and regulation of intracellular and intercellular signal transduction, to understand how cells talk to each other in the gastrointestinal (GI) tract, and to elucidate mechanisms and regulation of macromolecular transport (including nutrients, bacterial toxins, and viruses and viral product).

Mechanisms of Cellular Differentiation, Proliferation, Restitution, and Repair. These areas are the essential bases of healing once the intestine has been injured. Interesting and somewhat novel and surprising intracellular events in the intestine, liver, and pancreas need to be uncovered to better understand these processes.

Acid Peptic Disease. In pediatric acid peptic disease, development of cellular protection is poorly understood. Although a good deal of information exists regarding cellular protection in the human stomach, very little understanding exists about cellular protection in the human esophagus and no information exists about the mechanisms of cyto-protection of the developing or neonatal esophagus or stomach. For example, at least 40 percent of newborns reflux, but it is not known whether this reflux is a maladaptive response or whether humans need acid, enzymes, epidermal growth factor, or some other stomach-derived substance to stimulate production of protective mechanisms against infants' own acid.

***H. pylori*.** Research is needed to understand the role of *H. pylori* and other heliobacter infections on child health and disease; this is a childhood-acquired illness although the disease is

manifested in adulthood or adolescence. As a major pathogen in the United States and elsewhere, *H. pylori*'s impact on the GI tract needs to be examined. The basis and optimal therapy of reflux disease in pediatrics must be determined because primary studies of therapeutic agents are scarce and little is known about the interaction between motility and acid production in infants.

Endoscopy. Endoscopy is usually thought of as an invasive procedure but a number of adapted approaches need to be defined for children, including how to score the outcomes of endoscopy in children. Endoscopy in children is a clinical topic that is relevant to practice, to healthcare costs, and to the outcome of infantile reflux and *H. pylori* disease in infancy. New technologies that can be applied to pediatric interventions should be considered, such as endoscopic ultrasound and other tools and technologies that have not been widely applied (e.g., magnetic resonance cholangio-pancreatography [MRCP] and magnetic resonance imaging [MRI] of the biliary tract).

Cystic Fibrosis and Pancreatic Disorders. There has been an explosion of information about the genes involved in chronic and familial pancreatitis, in CF, and in the regulation of pancreatic development. Despite this plethora of information, it is not yet understood why the neonatal pancreas functions poorly and whether that poor functioning is adaptive or maladaptive for humans. The cell lineages of the endocrine or the exocrine pancreas is not yet understood in a way that allows clinicians to stimulate pancreatic growth or to re-synthesize the absence (genetically or from acquired disease) of pancreatic proteins. New diagnostics and therapies are needed for exocrine pancreatic insufficiency; coated enzyme preparations are not optimal. The clinical features of pancreatitis in children and adolescents need to be characterized, because little information exists and because this disease represents a significant number of emergency room visits in children's hospitals.

Motility Disorders. Motility disorders and functional GI states do occur in children; for example, reflux disease and irritable bowel syndrome. Clinicians see chronic abdominal pain in children as well as a lot of constipation – 20 percent of visits to pediatric clinics are for constipation. These problems are likely diet-related, although poor diet may be supported by poorly developed mechanisms of motility in certain predisposed individuals. Characterizing the pathophysiology, diagnosis, and treatment of pseudo-obstruction and cyclic vomiting would be important research goals, as these odd syndromes are seen frequently in children's hospitals and their basis is unclear. The development and regulation of gastrointestinal motility is an area of tremendous interest. A good deal of information is emerging in some centers regarding the enervation of the GI tract (particularly the colon) and the regulators that allow this to happen; however, the focus on development and its association with pediatric functional GI states has not been drawn sufficiently.

Biliary Atresia. Research on hepatic and biliary disorders has recently been stimulated by a Request for Applications (RFA) in biliary atresia and other liver diseases, but it is just a beginning. Research is needed to define the genetic and immunologic bases of pediatric liver diseases and to characterize the etiology and role of novel therapeutic interventions for formative hepatic failure. Little research has been conducted to date in this area, specifically for pediatric liver disease and defining the etiology and efficacy of therapeutic functions for extrahepatic biliary atresia. Clinicians see this disorder frequently in children's hospitals, although its

published prevalence is not high (about one-fifth as common as CF). An animal model exists for biliary atresia but research using that model has not uncovered many secrets yet. Hepatic and biliary disorders, including hepatitis in childhood, are areas of great research importance for the future.

Transplantation. The major goal at present is to understand immunologic and oral tolerance: to understand the capacity to induce tolerance and then use that understanding therapeutically to determine outcomes and treatments to prevent rejection, infection, and post-transplant tumors.

Obesity and Nutrition. Obesity remains a significant challenge in the United States today. The number of overweight and obese children continues to increase, and the genetic or physiologic determinants of childhood obesity are not yet understood. Safe interventions are needed that, in the long term, will prevent and treat childhood obesity. In addition, the efficacy and safety of "dietary supplements" (complementary and alternative products) need to be elucidated; approximately 30 percent of children admitted to children's hospitals have been exposed to or have participated in the use of complementary and alternative medicine.

Impact of Childhood Malnutrition. Research is needed to determine the impact of childhood malnutrition on diseases affecting adults, particularly IBD and other chronic diseases such as renal disease and liver disease. The RFA for the UO1 to elucidate the genetic basis of IBD will include children, but NASPGHAN would like more study of the genetic basis of pediatric IBD. For example, an interesting association on chromosome-5 with IBD beginning under age 16 should be investigated.

Microbial Flora. The role of microbial flora in the pathogenesis of IBD needs to be investigated. In some of the animal models, the absence of microbial flora in mutated immune models translates to an absence of IBD, indicating that research into the association of IBD with microbial flora is important.

Immune System. Research is needed to understand the role of the immune system, the mucosal barrier in early onset IBD, and nutritional and environmental factors in pathogenesis because of the overlap with the genetic background of the host. Level One evidence should be employed to develop optimal therapies for IBD in children and adolescents, an area in which the NASPGHAN hopes to partner with the consortium to move the research forward.

Allergy and Immunology. Research is needed to understand the mechanisms involved in oral tolerance, both for treatment and for the understanding of basic abnormalities. New approaches are needed to diagnose and treat food hypersensitivity reactions. The natural history and immunopathogenesis of Celiac disease must be understood, and approaches developed for early identification of genetically susceptible hosts. Research is needed to define the role of mucosal and systemic immune systems in malabsorption and growth, retardation, and congenital HIV, and in HIV of any kind that affects children.

Research Agenda, Specific Recommendations: Dr. Cohen

Dr. Cohen reiterated the NASPGHAN goals, in concert with the NIH, of making pediatric gastroenterology research requirements a top priority and to increase monetary support to promote research in pediatric gastroenterology. Specific recommendations to achieve these goals include establishment of pediatric gastroenterology centers of research excellence, SCORE or SPOR awards and cooperative agreements (U19 or U01 awards), and the recently successful example of the clinical research network RFA in biliary atresia. Pediatric gastroenterology centers do exist that are capable of responding to these kinds of requests.

The NASPGHAN would like to support the training of the next generation of experts in pediatric gastroenterology and to expand opportunities for training. Appropriate infrastructure already exists for this training, but training grant opportunities are needed. The Society would also like the nascent extramural pediatric research loan payment program continued and expanded, as it is likely to be a vibrant opportunity to attract researchers to the field.

Next steps are to plan future meetings to flesh out the details of the research recommendations contained in this research agenda within each relevant Institute's portfolio. In addition, new initiatives can be developed in partnership with the NIDDK, other NIH ICs, the FDA, and the Canadian Health Protection Branch within the Canadian Institutes for Health Research. Disease-related foundations, such as the Cystic Fibrosis Foundation and the American Liver Foundation, would also make excellent research partners for these initiatives. Dr. Cohen stated that the NASPGHAN wants to do everything it can to partner with the appropriate organizations to lend its expertise to promote these goals, including partnering with the appropriate industries.

In summary, Dr. Cohen reiterated the hope of establishing a significant partnership among the NASPGHAN, the CDHNF, and the NIH to make pediatric gastroenterology research a top priority.

Loan Repayment Update: Dr. Spiegel

Dr. Spiegel averred that the loan repayment program is the lifeblood of new investigators but it is a very small part of the NIH budget. Congress authorized four pieces of legislation, although no additional funds were appropriated to support these authorizations. Any money used for loan repayment would come out of grants, trials, and other NIH funding. Two of the loan repayment programs relate to health disparities research and individuals from "disadvantaged" backgrounds; both programs will be administered by the new National Center on Minority Health and Health Disparities (NCMHD). Investigators working on issues that qualify as health disparities might qualify for loan repayment under the NCMHD's program.

The two other programs authorized by Congress are the Clinical Research Enhancement Act and the Pediatric Research Enhancement Act. The Pediatric Research Enhancement Act would be reserved for pediatricians and for individuals conducting research on pediatric diseases. Both of these programs are being implemented this year (in Fiscal Year [FY] 2002). Subject to approval by the Office of Management and Budget, the applications will be available sometime in

December 2001. Applications will be available and accepted electronically via the NIH web site; applications will close sometime in February and will be reviewed in each Institute by groups of individuals (outside reviewers) who are on the training committees. These outside reviewers will make recommendations for funding to each Institute.

Acting NIH Director Ruth Kirschstein determined that the loan repayment programs should start as pilot programs, with approximately 250 loan repayment contracts offered NIH-wide in the first year. The maximum amount for an individual contract will be $100,000 and these contracts will be offered for 2 years. Eligible individuals would have loan indebtedness paid back at $35,000 per year for 2 years; since the average indebtedness of eligible individuals is approximately $80,000, many individuals will quality. The $100,000 maximum per individual is derived from the fact that this award incurs a tax obligation, so tax reimbursement will also be included. With regard to total indebtedness, the reviewers will not know the extent of the applicant's indebtedness. The NIDDK was allocated a minimum of 13 loan repayment awards for the current fiscal year (for a total of $1.3 million), but Dr. Spiegel added more funds to the NIDDK's program, thus increasing that number to a minimum of 20 awards (now totaling $2 million). More than 20 awards could be made if individuals' indebtedness is lower than the maximum.

The challenge ahead is how to apportion these awards across the various specialties and subspecialties. In the first year of the program, applicants must have some kind of NIH support to qualify for a loan repayment award. However, starting in FY2003, Dr. Kirschstein has committed to a variety of foundations that this program will be open more widely and applicants will not have to have NIH support. Because this program is not supported enthusiastically by some parts of the Federal Government, unless a compelling case can be made that the loan repayment money has served its purpose – to incentivize people to enter into research careers and to continue people already in research careers – the program could be in danger of discontinuance.

Dr. Spiegel suggested that the NASPGHAN provide appropriate demographic data – hard data about numbers of training slots available and how many of those positions remain unfilled in a given year. Pediatric specialties will have special consideration in this program since one bill of the authorizing legislation targets pediatrics.

Discussion about the career stage to which the loan repayment should be targeted has divided into two priorities. Some have argued that the program should be targeted early to people with training grants and to postdocs and fellows, with the rationale being to give incentives for going into research. However, a major concern is for the accountability problem that would arise if these young postdocs or fellows never actually go into a research career. On the other hand, some chiefs of medicine have made the case to target first-time RO1 holders for these loan repayment awards, making eligible those with T32, F32, most K (but not K24), and first-time RO1 and RO3 awardees. These researchers have already shown a commitment to the field and to research and, especially for those who do not win renewals of their awards, the loan repayment program might encourage them to continue in a research career.

Comments, Loan Repayment Program

One participant noted that targeting the loan repayment plan specifically to fellows might have a low return on investment because of the dropout rate; targeting individuals who have a K award is more reasonable.

One participant stated that few physicians are serving as elected representatives on Capitol Hill. Members of Congress who are physicians were trained in the 1960s and 1970s and they do not understand the importance of loan repayment. Most of the people on Capitol Hill do not understand what it is like to take a vow of poverty in order to go into research.

One participant stated that it is incumbent on everyone involved in the pediatric gastroenterology field, both at the NIH and outside the NIH, to advertise the loan repayment program to medical students and residents so they know that it exists.

One participant explained that it would be helpful to have a loan repayment program in place when beginning to develop investigator-initiated research and program projects focused on pediatric illness. RO1s and loan forgiveness can be a total package. Investment in pediatrics is investment in adult health: to prevent complications of IBD or other chronic illnesses in adults, researchers must assist clinicians in understanding the disease course in children. Investing in pediatric research pays off in knowledge about adult health – a message that has not always been well articulated to funding sources including industry.

General Comments and Q&A

Dr. Podskalny reported that an RFA is currently open for small research development centers (as opposed to the large digestive disease centers), including the desire to fund pediatric gastroenterology. The due date for applications is July 2002. Applications are expected to show a specific focus, for example, pediatric hepatology. The pediatric community is encouraged to apply for these grants.

One participant suggested that NASPGHAN advertise RFAs and other available funding opportunities by emailing its members to inform them about new RFAs and referring them to the appropriate web sites.

One participant announced that a new T32 program has begun in general pediatrics; pediatric gastroenterology applications will be accepted. The RFA has been available for several months and the due date is the end of January 2002.

Dr. Podskalny reported that, of the KO8 grants that have been awarded, there has been a decrease in the number of KO8s to pediatric gastroenterologists, from 37 percent in 1993-95 to 13 percent currently. In 1995, the Division had 14 postdoctoral positions in pediatric gastroenterology; that number has increased to 25. As the grant portfolio has increased to almost 200 postdoctoral slots, the proportion of pediatric positions has increased slightly from 10 percent to 13 percent.

Dr. Robuck reported that, with the nonalcoholic steatohepatitis (NASH) RFA, researchers of adult disease were strongly encouraged to collaborate with their pediatric colleagues to provide an opportunity to study NASH in children as well as adults. The applications have been read and many of them included pediatrics.

Regarding the biliary atresia RFA, Dr. Robuck noted that NASPGHAN helped to encourage quality applications. Neonatal hepatitis will also be part of this RFA. As data is collected on these children and because it will not be known at the outset whether they have biliary atresia or pediatric hepatitis, the opportunity will be available to gather data on a variety of pediatric liver diseases.

Dr. Robuck reported that the clinical RO3s have been removed from the regular DDKC committee; clinicians, pediatric gastroenterologists, and hepatologists have been added to that review team. The pediatric applications have fared well.

Dr. James explained that the IBD initiative is an RFA to form a consortium to study IBD genetics; those applications have just been received. Dr. Robert Karp, a geneticist, has recently been hired to play a major role in setting up this consortium. IBD is now being viewed as a possible model complex disease for development of large datasets, and several cooperative groups around the world are working on this problem.

Dr. Spiegel offered several comments:

- A trans-NIDDK planning group has formed and an RFA in GI development (stem cell biology) has recently been funded.
- A major beta-cell consortium is unraveling each step in pancreatic development and will study cascades, mouse models, and the relevant promoters.
- The NIDDK has a planning group in genetics, genomics, and bioinformatics. The IBD RFA has come out of that group, as has a co-funded (with the National Heart, Lung, and Blood Institute [NHLBI]) RFA on modifier genes in diseases that overlap the interests of the two Institutes – for example, CF. In support of its belief that modifier genes are critically important, the Institute will offer its own RFA, funding permitting, in which researchers will investigate a broader spectrum of relevant diseases.
- It is important that this research agenda be discussed with other ICs, for example, the National Institute of Child Health and Human Development (NICHD).

In response to the question of how NASPGHAN can begin to dialog with other ICs, an NIH participant responded that NASPGHAN should contact members of the DDICC committee. In addition, they can share the summary generated from this meeting with other relevant ICs and use the summary to begin discussions.

Dr. Winer explained that the NICHD's 10-year-old Child Health Research Center funds 20 pediatric departments around the country. Those pediatric departments provide funding to between 2 and 4 scholars (junior faculty members) for 2 or 3 years, funding that is earmarked for the transition period between the K award and the highly competitive R awards. Pediatric gastroenterology represents a small percentage of the trainees; because the principal investigator of each grant is the chair of pediatrics for each of these institutions, the final funding decision is

made by that person. She also explained that the NICHD's T32 program is just beginning; the RFA is out and the receipt date is in January 2002. This grant can support clinical research or basic research, the principal investigator must be the chair of pediatrics, and pediatric GI can be the sole focus. The NICHD also has cooperative agreements, using the U10 mechanism through the perinatology branch, that produce neonatal research, are clinically oriented, and conduct some gastroenterology research.

One participant commented that the CDNHF could identify potential areas of RFAs or research and then provide that information to its members on a timely basis. The CDNHF web site could provides links to the NIH as well as information about and assistance in applying. While the NASPGHAN/CDNHF is pursuing the research agenda, it can also play an active role in facilitating applications in order to stimulate more pediatric GI research.

One participant elaborated on the NIDDK's process for conceptualizing initiatives. By NIDDK's May council meeting, some initiatives and concepts for initiatives have already been enumerated for the following fiscal year; they are posted on the NIDDK web site. By the September council round, that list has been winnowed and published in a more detailed form. NASPGHAN could pick up those potential initiatives and concepts at an early stage and ensure that its membership is aware of them, with the disclaimer that they are not guaranteed to receive funding.

One participant noted that specific ideas from NASPGHAN members would also be helpful. Under discussion (and needing feedback from the field) are potential RFAs on GI motility, hemolytic-uremic syndrome (HUS) and foodborne illness, and hepatocyte cell transplantation.

One participant informed the DDICC that a meeting is planned tentatively for September 2002 on innovative approaches to treatment of inborn errors of metabolism and hereditary tyrosinemia.

One NASPGHAN participant remarked that NASPGHAN recognizes that it is not the NIDDK's only constituent but that it does want to be an important constituent. The Society wants to partner with the NIH – not only with regard to funding but also to publicize information to its membership about how to be responsive to funding opportunities.

In answer to a query about what the NIDDK views as healthcare disparity issues (minority issues) affecting children in pediatric gastroenterology, two NIDDK participants responded with the following list: end-stage renal disease (ESRD), Type 2 diabetes, *H. pylori*, gallstones, HIV, hepatitis, and obesity. One participant noted that the NCMHD has an increasing budget and has proven an effective partner with the NIDDK in a number of areas.

One participant described a major initiative on Type 2 diabetes in children, including a treatment arm with a number of centers and a prevention arm. The prevention arm deals primarily with obesity-related issues and therefore both relevant divisions are working together on this initiative.

One NASPGHAN participant explained that the Foundation offered a nutrition award for clinical research related to obesity. Because there is little understanding of the cause, treatment, and epidemiology of childhood obesity, this topic would be a reasonable RFA for a clinical center. He suggested that obesity in children might present a brainstorming issue that could cross NIH IC boundaries by dealing with disparity issues; NASPGHAN may be able to partner with the NIH in this area.

One NIDDK participant stated that this is an area that NIH is pursuing vigorously, from genetic and environmental standpoints. A major RFA is scheduled to come out on environmental approaches to obesity prevention. About two years ago a trans-NIH pilot project effort on innovative approaches to obesity prevention began; results are currently under review. One example of this pilot project was a program in which children agreed only to watch television while on stationary bikes; the result was that all these children lost weight and they all watched much less television.

Dr. Hoofnagle mentioned the issue of obtaining assistance from and partnering with industry. He explained that the NIDDK had hoped that some of its networks, particularly biliary atresia, might stimulate donations from private individuals or industry.

Adjournment

Dr. Hoofnagle thanked the NASPGHAN/CDHNF participants and the DDICC committee members and adjourned the meeting.

Approved by: _____ Date: _____
Jay H. Hoofnagle, M.D., Chair
Digestive Diseases Interagency Coordinating Committee, NIDDK

Approved by: _____ Date: _____
Stephen P. James, M.D., Executive Secretary
Digestive Diseases Interagency Coordinating Committee, NIDDK

Appendix 1:
Committee Roster

[Please insert full committee roster with names, addresses, telephone and fax numbers, and email addresses.]

Appendix 2:
List of Acronyms

CDHNF	Children's Digestive Health and Nutrition Foundation
CF	cystic fibrosis
DDIC	Digestive Diseases Interagency Coordinating Committee
ESRD	end-stage renal disease
FDA	U.S. Food and Drug Administration
GI	gastrointestinal
HUS	hemolytic-uremic syndrome
IBD	inflammatory bowel disease
ICs	NIH Institutes and Centers
MRCP	magnetic resonance cholangio-pancreatography
MRI	magnetic resonance imaging
NASH	nonalcoholic steatohepatitis
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
NCMHD	National Center on Minority Health and Health Disparities
NHLBI	National Heart, Lung, and Blood Institute
NICHD	National Institute of Child Health and Human Development
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
PHIS	pediatric health information system
RFA	Request for Applications