Redefining Genetic Disorders
Wendy Chung and Ron Wapner
Wield New Diagnostic Tools

In medical genetics, a patient who is “n of one” is the first and only person in the world diagnosed with a particular genetic disorder. With new diagnostic tools like chromosomal microarray and exome and whole genome sequencing, pediatrician and geneticist Wendy Chung, MD, PhD and frequent collaborator Ron Wapner, MD, a geneticist in maternal-fetal medicine, are discovering a remarkable number of “n of ones,” Dr. Chung says. Together they are working to understand the impact of rare genetic disorders on developing fetuses and growing children, and on their...

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Beyond Antibiotics
Alice Prince Probes the Host Immune Response to Infection

Antibiotic-resistant “superbugs” have sparked an intensifying effort by the government, pharmaceutical companies, and academic researchers to develop new antibiotic drugs that can wipe out these pathogens during an infection. CUMC researcher Alice Prince, MD is working toward potential treatments through a different approach: she and members of her laboratory are teasing apart the complex of immune reactions that occur when the host’s body encounters a pathogen. “We still have several antibiotics that can kill MRSA (methicillin-resistant Staphylococcus aureus) in vitro, but what we can’t control is our own immune response to the bacteria,” she says.

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Message from the Editors

Research remains integral to academic medicine. Through basic research we define key questions about the natural histories of, and treatments for, patients’ diseases. In translational research we develop and use animal models to understand these diseases more fully. And clinical research allows us to pose and answer questions that affirm or change the care we provide. The physician-scientists in both our departments are deeply familiar with the clinical problems they’re studying, and are remarkably collaborative both within their departments and with researchers in other departments. In this issue of Connections we showcase two important research initiatives: pediatrician Dr. Wendy Chung and perinatologist-obstetrician Dr. Ron Wapner are working together to determine how newly discovered genetic diseases affect patients as they grow, and Dr. Alice Prince and her research team are probing the role of the immune response in bacterial infections. This issue also includes a profile of Pediatrics’ Vice Chair of Faculty Development Dr. Susan Rosenthal, as well as stories about a program that enables families to stay with babies whose lives last only minutes, hours, or days; a new bone mineral density analysis offering for children; and our biochemical genetics program. Our next issue will look at the many ways that we make use of technology in providing care to our patients—stay tuned!

Michael Weiner, MD
Department of Pediatrics

Cande Ananth, PhD, MPH
Department of Obstetrics and Gynecology

Co-Editors-in-Chief

Connections
Dr. Wapner has also spearheaded a perinatal Fetal Medicine Units network, which is funded to belong to large networks including the Maternal-questions to affirm or change clinical care. We junior investigators.

Our phenomenal administrator, Michelle DiVito, has built a terrific administrative team to help clinical trials and clinical research projects with Dr. Ron Wapner, who has structured large-scale seven years we have created a structure for re-search and appointed a vice chair for research, under Ron’s leadership primarily we have ap-plied for more grants to more NIH institutes. We’ve also invested a very significant amount of our philanthropic efforts into supporting young investigators, and have been able to recruit and support a number of young faculty until they become productive, independent scientists. We’re also advocating for an increase in funding for training grants for young faculty from three to five years, because we believe it takes up to five years in the current environment to make somebody competitive. So we are using every possible mechanism to preserve our research mission.

Dr. Stanberry: We also invest in talent, whether it’s junior or more senior researchers. Over the last five years we’ve invested heavily in recruiting talented leaders in research as well as promising young investigators, and even with the shrinking NIH budget we’ve seen about a doubling of our NIH funding during that time. So while it’s really been a very bleak picture for the country, and looks to be even more bleak going forward, there’s still billions of dollars out there that are going to go somewhere to support research. Our view is that that money should be coming here. And we’ve certainly, in both departments, had considerable success in growing our NIH research over the past five years.

Dr. Stanberry: I think success breeds success. And I feel that the unique collaboration that our two departments enjoy, and that we enjoy with many other departments, makes us more attractive for multidisciplinary grants. We enjoy collaborations with pediatric cardiology, with Dr. Chung’s group in genetics, with Dr. Polin in neonatology. Having the spectrum of women’s health from prenatal to postnatal life is extremely powerful.

Dr. Stanberry: Columbia’s a remarkably collaborative institution, which enables us to work with talented people in other departments to create big science, or to create collaborations that would not develop in other settings. People want to come here; this is an exceptional place to do research.
Finding New Ways to Prevent Reproductive Tract Infections

Reproductive tract infections (RTI) are a major cause of both preterm delivery and early-onset sepsis in newborns. Infectious disease researcher Adam Ratner, MD, MPH and colleagues are devising a new, non-antibiotic strategy to prevent the two most common RTIs, bacterial vaginosis (BV) and group B Streptococcal (GBS) infection. Gardnerella vaginalis (the major constituent of the vaginal microbiota during BV) and GBS form biofilms that enable them to, in some cases, colonize the mucosal surface of the vagina over a long period. These biofilms contain bacteria embedded in a matrix of proteins, polysaccharides, and extracellular DNA. Because extracellular DNA can be degraded by the enzyme DNase, Dr. Ratner and his group have hypothesized that using a DNase gel intravaginally could decrease the risk of these RTIs in late pregnancy. The group is formulating DNase gel prototypes and evaluating their effectiveness against RTIs, and is also developing behavioral instruments to study microbicide acceptability in pregnant women. Once the team has identified a lead gel candidate, they plan to expand their efficacy and toxicology studies in vivo, and will study the acceptability of the gel among locally and nationally representative populations of pregnant women. If they identify an effective, non-toxic gel, they hope to move on to clinical studies. Other lead investigators involved in the project include CUMC’s Lawrence Stanberry, MD, PhD and Susan Rosenthal, PhD, as well as Shari Gelber, MD (Cornell OB/GYN), Russell Mumper, PhD (University of North Carolina at Chapel Hill’s School of Pharmacy), and Gregory Zimet, PhD (University of Indiana).

Fecal Implant: A New Approach to Treating Children with C. difficile

The incidence of Clostridium difficile (C. difficile) infections in children has increased dramatically over the last 20 years (2.6 in 1991-97 to 32.6 per 100,000 person-years in 2004-07, according to a recent study), and children with this infection frequently suffer debilitating diarrhea, weight loss, and bloody stools. Relapses after standard antibiotic treatment are common, occurring in an estimated 20-30% of patients, and with more frequent relapses, the chance of successful eradication of the infection diminishes. Fecal microbiota transplant (FMT), a procedure in which stool from a healthy donor is infused into the gastrointestinal tract of a recipient, is the subject of ongoing study and, in adults, has been shown to be approximately 90% effective in curing relapsing cases. Only isolated patient case reports have been published in children. Faced with a young patient who had experienced years of C. difficile relapses, who could not be weaned off of antibiotics and required indefinite antibiotic treatment to be permitted to attend school, Norelle Rizkalla Reilly, MD devised a protocol based upon previously published protocols for FMT. Since early 2012 (often in collaboration with pediatric gastroenterologist Ali Mencin, MD), Dr. Rizkalla Reilly has treated six children with relapsing C. difficile infections using this protocol, and in all of the children the procedure was successful. She presented the protocol and findings at the Intestinal Immune-Based Inflammatory Diseases Symposium Patient Program in March 2013. Dr. Rizkalla Reilly is in the process of publishing the findings in children, and is exploring opportunities for translational research.
Robotic versus Laparoscopic Hysterectomy: Which is Better?

Over the last decade robotic surgery for hysterectomies has increased dramatically. Each year approximately 600,000 American women have hysterectomies, according to the Centers for Disease Control and Prevention. By the time they reach age 60 a third of American women have had their uteruses removed. Since the Food and Drug Administration’s approval of robotic gynecologic surgery in 2005 the procedure has been heavily marketed but little is known about its purported benefits compared to the more common laparoscopic method. While the two procedures have similar complication rates, robotically-assisted surgery for hysterectomy costs, on average, about one-third more than laparoscopic surgery, according to new study by Jason Wright, MD, and his colleagues in the Department of Obstetrics and Gynecology. (The costs for robotic hysterectomy averaged $8,868 versus $6,679 for laparoscopic hysterectomy.) OB/GYN researchers analyzed data on 264,758 women who had hysterectomies for non-cancerous conditions at 441 hospitals across the US from 2007 to 2010. The findings, published in the Journal of the American Medical Association, found that use of the robotic technique grew from 0.5% of operations studied in 2007 to 9.5% by early 2010. “We noted that despite almost no data the use of robotic hysterectomy by physicians increased dramatically,” said Dr. Wright, Levine Family Assistant Professor of Women’s Health and the study’s lead author. “The data raises a lot of questions and patients should talk to their physician to weigh the outcomes and compare the cost,” he added. He and his colleagues found that women who had the robotic operations were slightly less likely to spend more than two days in the hospital, but that overall complication rates were the same for both groups. “Our findings highlight the importance of developing rational strategies to implement new surgical technologies,” the researchers wrote.


Risk of Uterine Rupture and Placenta Accreta Minimal in Women with Prior Uterine Surgery

Some OB/GYNs have moved delivery for women with a prior classical cesarean or prior myomectomy into the late preterm period to avoid the theoretical risk of uterine rupture before labor begins. A study by Cynthia Gyamfi-Bannerman, MD, an Associate Professor in OB/GYN, found that a prior myomectomy (surgical removal of uterine fibroids) is not associated with higher risks of either uterine rupture or placenta accreta. The study, under the aegis of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network, published in Obstetrics and Gynecology, evaluated 176 women with a prior myomectomy, 455 with a prior classical cesarean delivery, and 13,273 women with a prior low-segment transverse cesarean delivery. The study found that the absolute risks of uterine rupture and accreta after prior myomectomy are low due to practice patterns that include measures to prevent uterine rupture and other complications. The study also found that women with prior myomectomy or prior classical cesarean delivery were significantly more likely to be African-American, whereas those with a prior low-segment transverse cesarean delivery were more likely to be Caucasian. Finally, women with a prior low-segment transverse cesarean had the highest mean gestational age at delivery and were the most likely to have labored. These findings run contrary to current obstetrical practice, where women with a prior hysterectomy are often delivered by cesarean before 39 or even 37 weeks to prevent uterine rupture. “These data showed that you can deliver them at 38 to 39 weeks,” Dr. Gyamfi-Bannerman said. The findings have the potential to change standards of care. Dr. Gyamfi-Bannerman and her team advocate against delivery before 37 completed weeks because of the morbidity associated with late preterm birth and little objective supporting evidence for delivery prior to this time.

When Susan Rosenthal, PhD was recruited as Vice Chair of Faculty Development four years ago she didn’t expect that her job description would expand just 2.5 years later to include Director of the Division of Child and Adolescent Health. Add to these two assignments her active NIH-funded research portfolio, and Dr. Rosenthal juggles many responsibilities.

The division Dr. Rosenthal oversees includes five distinct practices: General Pediatrics, Adolescent Medicine, Child Maltreatment, Development and Behavioral Pediatrics, and Pediatric Hospital Medicine. “Some of these sections are currently pretty small,” she says. But each has its own distinctive mission. “As a division director you manage not only clinical care, teaching, and research—but in this case manage them in very different clinical delivery systems. So even though the adolescent specialists practice in the same clinic with the general pediatricians, an adolescent medicine visit is different from a general pediatric visit and we have different productivity standards.” Dr. Rosenthal says her “amazing Associate Division Director, Pat Hametz, MD, MPH,” really helps her direct the diverse activities of the group.

Dr. Rosenthal’s division is on a long-term growth plan, she says. “One of my goals is to promote the many really important, interesting research, teaching, and clinical activities the division’s faculty are doing, and leverage them so that we can continue to be innovative, and enhance our national reputation.” As an example, Dr. Rosenthal notes that CUMC provides clinical care in a primary care setting to many children who are seriously ill with chronic, complex medical conditions, complicated by psychosocial stressors in their lives. “And the pediatricians do a great job of it,” she adds. To elevate the care of these children and their families to the next level, Adriana Matiz, MD, Medical Director of the Washington Heights Family Health Center, is developing a medical home model—team-based care led by a physician who oversees continuous and coordinated care for each patient.

Dr. Rosenthal’s recruitment to drive faculty development represented a shift in focus in the department, she says. “Dr. Stanberry is interested in ensuring that faculty members are promoted within the department and are academically successful, so we are helping faculty members get recognition for what they’ve already accomplished and then build on those accomplishments in a systematic way.” One of her first changes was to ensure that faculty meet regularly with their division directors to talk about their careers, goals, and long-term plans, “so that they could make good decisions about how to spend their precious time,” she says.

Four years ago she instituted an annual faculty review, a formative evaluation that focuses the faculty and division director on ensuring that there is an agreement and a plan for career growth and academic focus. The review system is now web-based, allowing Dr. Rosenthal to use the forms to provide feedback to department leadership and faculty and to make appropriate changes. When faculty members were asked to list their mentor and their mentee when the review was initiated, for example, “there was a real mismatch,” she says. “People were listing mentors who weren’t their mentee or listing mentees who weren’t their mentors. And so the next year, we said, it’s really important that you have the conversation with the person and you both agree what your expectations of each other are.”

Dr. Rosenthal also developed a highly regarded year-long leadership program (see article in Connections Issue 1), and is in the process with Dr. Hametz of creating a pediatric residency leadership curriculum. “We’re going to start really thinking about leadership training from the residency program on through to the faculty.” She has also instituted a “Lunch with the Chair,” where every few months 10 faculty members have an opportunity to talk to Dr. Stanberry in an informal setting. The department now has an orientation for new faculty followed by a reception to welcome them and congratulate others who have been promoted. “We’re looking for ways to expand and increase these kinds of interactions because the pediatric faculty is geographically spread out, and there’s no place where we come together in one setting to meet, greet, and chat.”

Dr. Rosenthal’s research focuses on promoting sexual health and preventing sexually transmitted infections (STDs) in adolescents and young adults. Through one of her two current primary grants, she is examining the parent-adolescent conversations that take place when adolescents are offered the opportunity to enroll in clinical trials of STD preventive methods. “We are presenting adolescent boys and girls and their parents with a hypothetical study involving the safety evaluation of a potential topical microbicide. We ask adolescents if would they be willing to participate, and parents if they would let their adolescent participate, and then we ask them to discuss the possibility of participation together.”

In another study Dr. Rosenthal has teamed up with infectious disease researcher Adam Ratner, PhD, who is developing new methods to prevent bacterial vaginosis (BV), one of the leading causes of premature birth. “The question I am researching is: if he developed a topical microbicide to be used during pregnancy to prevent bacterial vaginosis, would women be willing to use it?” The research team is interviewing pregnant women in their last trimester about the kinds of behavioral changes they make during pregnancy for the baby and themselves, and their willingness to use a gel to prevent BV.

While Dr. Rosenthal’s three job titles and their attendant responsibilities seem very diverse, in fact there is high overlap, she says. “What I know about developing faculty helps me understand how I can work with my division members—those two jobs feed back and forth into each other. And being a psychologist and behavioral researcher has really informed the faculty development—it’s helped me understand that I need to collect data systematically, and how to promote leadership. In one sense I feel like I have three completely different jobs, yet they all compliment each other.”

—Beth Hanson
CUMC specialists rely increasingly on a new diagnostic shortcut: whole exome sequencing.

The Norwegian doctor Asbjörn Fölling was the first to trace the roots of a patient’s severe intellectual disability to a metabolic disorder, a disease in which the body can’t break down or use proteins, fats, or carbohydrates. Dr. Fölling’s insight in 1934, that a severely disabled young brother and sister were unable to metabolize the amino acid phenylalanine, paved the way for the discovery of dozens of other metabolic disorders in the many decades since. The siblings had phenylketonuria or PKU, the most common metabolic disorder, which today is controlled through a diet free of phenylalanine starting at birth. Babies born in the developed world are now universally screened for a number of metabolic disorders, some of which can be controlled through enzyme infusions, medications, or special diets.

A recent development in the diagnosis and treatment of metabolic disorders is molecular testing, says biochemical genetics specialist Alejandro Iglesias, MD. Over the past year Dr. Iglesias has made increasing use of a specific molecular testing approach. “When DNA-based diagnosis is needed, instead of looking at all of the genes and sequencing the entire genome to arrive at a diagnosis, which is quite complicated and expensive, we now use a ‘short cut,’ and look at small pieces of the genes—the meaningful ones—and the technique is giving a high yield.” The new approach, called whole exome sequencing (WES), looks only at the regions of the genes that encode the proteins, making it faster, easier, and cheaper to arrive at a definitive diagnosis, and to begin the best treatment. The technique has a few shortcomings, but is so far very cost-effective, Dr. Iglesias says. “We are just starting to do this in-house, allowing us to provide testing to an increasing number of patients,” he adds. “In a short period of time this has become more doable and has given us a powerful diagnostic tool.” Dr. Iglesias foresees the possibility of using whole genome sequencing in the near future. It’s doable now, he says, but is still extremely expensive and very difficult to interpret. In time, “we will have an even more powerful tools to help our patients.”

With Dr. Iglesias’s arrival in 2011, CUMC established its Biochemical Genetics Program, and is now one of nine state-designated treatment centers for diseases such as cystic fibrosis, sickle cell anemia, PKU, and other errors of inborn metabolism in New York. The state provides screening for more than 40 congenital disorders and HIV exposure within 48 hours of birth for the 350,000-plus infants born in New York each year. If the screening detects a metabolic disease, infants and their families are referred to the nearest designated treatment center.

The members of CUMC’s Biochemical Genetics Program offer a multidisciplinary approach geared toward each patient’s metabolic condition. The team includes a metabolic nurse, registered dietitian, social worker, and genetic counselor, and depending on the patient’s condition may also include gastroenterologists, cardiologists, neurologists, orthopedic surgeons, ophthalmologists, pulmonologists, and transplant surgeons. Together the group provides dietary management, enzyme replacement therapy and, in advanced cases, bone marrow, liver, kidney, or heart transplantation.

Patients with a particular group of disorders called lysosomal storage diseases (Pompe, Fabry, and Gaucher diseases are among the most common) can be treated with enzyme replacement therapy (ERT). This is usually very effective, Dr. Iglesias says. “We replace what they don’t have with enzyme infusions.” Devising a specialized diet can help lessen or prevent the serious side effects of many of the other disorders, particularly if the diet is started before the baby shows any sign of the disease. “With babies this is easy,” he adds. “You just use a specific formula. When they get older you have to find the foods that are low in this or that substance, and we often add vitamins and supplements.” While PKU can be very successfully controlled through diet, control is more complicated and difficult with other disorders, and over the last 40 years treatments for these diseases have been based on the same principles, “so we are constantly looking for better ways to treat our patients,” says Dr. Iglesias.

Metabolic disorders are rare: PKU affects just one of every 10,000 people. “In our field, if we see a few patients, somehow we see most of them,” Dr. Iglesias says. But because these diseases are so rare, “it’s hard to find funds for research,” he adds, and it’s also difficult to find enough patients to enroll in clinical trials. Some new treatments in development that might some day change the course of these diseases include gene therapy and infusions of healthy cells, such as liver cells, which can migrate to the liver and take over the function of the diseased cells.

In addition to patients with metabolic disorders, Dr. Iglesias also cares for children with other genetic diseases including Down syndrome, Turner syndrome, and congenital heart problems.

— Beth Hanson
Osteoporosis is a staple of conversations among the elderly and AARP articles, but it’s a term rarely heard during a pediatric visit. However, for children with certain medical conditions and those who take specific medications, low bone density and the subsequent risk of fracture is a real and immediate concern. While testing of bone mineral density (BMD) in adults is a well-established field, determining BMD in children requires specific expertise and training. Early this year two pediatric endocrinologists with just such expertise initiated a new program offering bone density testing for children and adolescents in CUMC’s Toni Stabile Metabolic Bone Disease Unit.

The program is the outcome of many years of planning between the Adult and Pediatric Endocrinology Divisions and the joint vision and collaboration of John Bilezikian, MD, Director of Adult Endocrinology and Sharon Oberfield, MD, Director of Pediatric Endocrinology, Diabetes and Metabolism. Their goal was to provide bone mineral density interpretation “from cradle to adulthood.” To achieve this, both Ilene Fennoy, MD, MPH and Aviva Sopher, MD, MS have been certified to interpret pediatric bone density by the International Society for Clinical Densitometry (ISCD). “Before this year, the BMD tests of children or adolescents who were referred for testing at CUMC were evaluated by endocrinologists who treat adults, and who were not necessarily familiar with the issues associated with pediatric bone mineral density,” Dr. Sopher says.

Among the many causes of concern about a child’s bone health is chronic steroid use, a special problem among children with inflammatory conditions. “We see many children with lupus, other rheumatologic, gastrointestinal, and oncologic disorders who receive large doses of steroids for long periods of time, which can have detrimental effects on the bones,” Dr. Sopher says. “Physicians may want to obtain a baseline BMD to enable them to compare the density of the bone before and after steroid therapy.” Because of steroids’ global anti-inflammatory effects, “chronic steroid use can be encountered in many of the subspecialties in pediatrics,” adds Dr. Sopher.

Children with bone disorders such as osteogenesis imperfecta, a rare genetic defect in bone formation, can develop multiple fractures during childhood. They also undergo periodic bone density testing. Dr. Fennoy oversees infusion therapy for children with osteogenesis imperfecta, in which they are treated with intravenous infusions of bisphosphonate to strengthen their bones, says Dr. Sopher. “Then we monitor the effectiveness of the treatment with the bone density testing.”

BMD testing might also be ordered in children with medical issues that increase the risk of low BMD such as girls with anorexia nervosa and boys with Klinefelter syndrome, a chromosomal disorder associated with low levels of testosterone, according to Dr. Sopher.

Bone mineral density is measured using a technology called dual-energy X-ray absorptiometry or DXA. During the procedure, the DXA machine aims two X-ray beams with different energy levels at the bones. BMD is determined by subtracting out the absorption of soft tissue and calculating the bone’s absorption of each beam. Both children and adults are assessed using the same machine, but technicians use different settings depending on the size of the patient, explains Dr. Sopher. She and Dr. Fennoy generally recommend whole body and spine studies for children and adolescents. The results of each test are compared to reference standards for normal bone accrual, which were gathered as part of the Bone Mineral Density in Childhood Study, a multicenter, NIH-funded longitudinal study of 1,554 healthy children and adolescents between the ages of 6 and 16 years; Dr. Oberfield was the Columbia University Site Director for this research.

The DXA technology also has applications outside of BMD testing. “Many people don’t realize that you not only get bone density but also get full body composition during testing, so we can determine percentage body fat, lean body mass, and determine where the fat is located. If you have more in the abdomen, for example, this is associated with risk for metabolic syndrome and insulin resistance,” Dr. Sopher says.

She and Dr. Fennoy are planning to use bone density data in some of their research studies. In one study Dr. Sopher will look at adolescent girls with polycystic ovary syndrome (PCOS), who don’t have regular menstrual cycles, and are exposed to lower levels of the hormone estrogen than girls with regular periods. Her study aims to determine whether lower hormone exposure leads to bone density differences in adolescents with the syndrome. Girls with PCOS may also accumulate fat in their abdomen and liver, “which can lead to insulin resistance, so we can use DXA to measure the percentage of body fat, and get an overall idea if there is excess fat or not,” she explains.

In another research project, Dr. Fennoy and Marisa Censani, the current fellow in Pediatric Endocrinology, are using DXA to study BMD changes after bariatric surgery (gastric sleeve surgery) in morbidly obese adolescents; they are evaluating patients’ BMD before and after the procedure, says Dr. Sopher. Their hypothesis is that BMD will decrease following the surgery, “but we don’t know and hope that the study will provide answers.” Dr. Sopher and Dr. Fennoy have IRB approval to create a database of BMD and body composition related information of patients referred for DXA and who agree to participate. The data will be an extremely useful addition to current knowledge about pediatric bone mineral density and body composition.

Before CUMC established its pediatric BMD testing program patients here were sent elsewhere for testing. “Obviously it’s an inconvenience if patients are receiving all of their care here at Columbia, and then have to go to another institution for bone mineral density testing,” says Dr. Sopher. “So looking forward we thought that it would make sense to bring the bone density testing and our knowledge in pediatric bone density here and have it all available at CUMC.” Drs. Fennoy and Sopher currently interpret about three or four BMD tests each week, and expect those numbers to rise as doctors from all pediatric subspecialties learn that BMD testing is now available here at CUMC.

— Beth Hanson
A baby’s birth awakens tenderness, affection, joy, wonder, and dreams of a long and full life. What can we do for infants and their families when a new life lasts only minutes, hours, or days? A few years ago neonatologist Elvira Parravicini, MD was moved by the plight of two women who knew their babies would be born with the life-limiting condition trisomy 18, but who wanted to carry and deliver them anyway. Dr. Parravicini helped these parents have a meaningful, if brief, time with their babies, and has since created a role for herself and a collaborative team of caregivers to provide what is called comfort care for babies who live for only a short time after birth.

About 15 babies each year are born at CUMC with life-limiting conditions; the most common are trisomy 18, in which a baby has three copies of the 18th chromosome, and Potter’s syndrome, where babies are born with no kidneys and very small lungs. “I found myself following these cases,” Dr. Parravicini says, “and then some nurses, social workers, and child life specialists in pediatrics also became interested.” The collaborative program she has developed involves maternal-fetal medicine specialists, geneticists, delivery room and NICU nurses, social workers, and child life specialists, who work together to counsel parents prior to delivery and offer them a complete plan for making the most of their short time together.

Dr. Parravicini and her team have developed what she calls detailed pillars of comfort care. “Nowadays many professionals use the expression ‘comfort care’ to mean ‘don’t do anything,’ which is not what we offer,” she says. “A baby wants to be warm, wants to be held, wants a full tummy, and to be free from pain.” Dr. Parravicini gives mothers the option to do “kangaroo care” in the delivery room, a technique in which the mom holds the baby skin-to-skin against her chest, and her body temperature increases in order to warm the baby. “These babies are going to have a short life, and this is such a beautiful way for a parent to bond with them,” she says. Babies are also given milk, not with the goal of growth, but just so they have a sense of satisfaction and a full stomach, and if they appear to be in pain, it is managed.

A NewYork-Presbyterian Patient Centered Care Grant enabled Dr. Parravicini to furnish one of the rooms in the NICU to use for comfort care cases, and parents and other donors provided a crib, baby tub, blankets, and clothes. “The family can get together either in this room, in the delivery room if the baby expires shortly after delivery, or on postpartum ward if the baby is full term and doesn’t need additional care,” she says. If the baby is expected to live for some time the team can plan transfer to another facility or hospice care at home. “We put the family in touch with a network so that they don’t have to face the death of their baby on their own.”

CUMC child life specialists work with the baby’s siblings, helping them understand and come to terms with the baby’s life and death. “Sometimes parents try to hide from older siblings that their little brother or sister is dying. Our child life specialists are very much involved in helping the family face this together, because it is something you cannot hide—it’s part of their life,” says Dr. Parravicini.

In reflecting on how meaningful this experience can be, she says, “It’s incredible that some parents who are expecting babies like this want to have a Caesarean section so that they can have a live baby to hold. You want to say, ‘the baby is going to die, so why do you have to go through a C-section?’” Dr. Parravicini tells the story of a woman in her forties whose baby was diagnosed prenatally with Potters syndrome. “She said, ‘I want to enjoy this. This is the only chance I will have to be a mother.’” So she carried the baby to full term and “kangarooed” the very tiny baby for seven hours until he died. “Everybody in the delivery room was very moved,” Dr. Parravicini says. “It was beautiful.”

It is a terrible situation when parents lose a child, she adds. “But these parents are very thankful because by doing all of this you allow them to stay with the baby, even if it’s for just a few hours. It possible to see a lot of humanity during this time. This is so much better than having the baby taken away.”

— Beth Hanson
Babies Heart Fund

Saving & Improving The Lives of Children With Heart Disease

Learning that your newborn has a cardiac abnormality is one of the toughest things for new parents to hear—but for decades faculty in the Division of Pediatric Cardiology have helped allay those fears, and continue to provide the very best care for the youngest and most vulnerable patients.

To ensure that this high level of care continues to improve and is available to all children, in 1986 a group of families started the Babies Heart Fund. The Fund was conceived when a group of families with young children who were helped by doctors in the Division gathered over Sunday brunch to talk about how best to give back. Since then the Fund has grown into a vital force that brings families together and provides generous support to Pediatric Cardiology throughout the year.

On February 14, 2013, the Babies Heart Fund held its 26th Annual Gala at Cipriani 42nd Street. About 350 partygoers attended the Valentine’s Day celebration and participated in an exciting silent auction; attendees donated more than $450,000 to the Fund. Guests received the book Friends Help Hearts Heal, by patient Harry Zuckerman and his friend Kyle Pearlman. The boys were featured in the Gala video along with honoree E. Robert Roskind, one of the founders of the Babies Heart Fund and its chairman for many years. It was a "heartfelt" evening to say the least.

Robert Roskind also announced his family’s efforts to establish the Division’s second professorship—this one in honor of James R. Malm, MD, who performed both of his son Scott's successful childhood surgeries. Scott Roskind is now the father of two, and has succeeded his father as co-chair of the Babies Heart Fund with grateful parent, John Minio.

Proceeds from the Babies Heart Fund were originally directed to support the training of our fellows—the young doctors who will become leaders in pediatric cardiology. The mission of the Babies Heart Fund recently expanded to support not just medical training, but also innovative research that will help us understand the cellular and molecular mechanisms that cause heart disease in children.

We are so grateful to the Babies Heart Fund for supporting the Division of Pediatric Cardiology's exceptional clinical care and its pioneering research, which enables us to provide our patients with the best possible outcomes. —John Danziger
NewYork-Presbyterian/Columbia’s CHALK Program Takes to the National Stage

Five years ago doctors and healthcare workers at NewYork-Presbyterian/Columbia and its Ambulatory Care Network got together to share their concerns about the prevalence of childhood obesity and its related morbidity in Northern Manhattan, and established a program called CHALK (Choosing Healthy & Active Lifestyles for Kids). Today, the CHALK/Just Move effort is making national headlines as one of three model programs chosen for First Lady Michelle Obama’s new campaign, Let’s Move! Active Schools.
The First Lady’s initiative, announced at a rally and press conference in Chicago in late February, is designed to bring physical activity back to the nation’s schools. “This is about giving our kids the structure and support they need to thrive in every single aspect of their lives,” said Mrs. Obama at the kick-off event. “It’s about giving them something to strive for, something to hope for, somewhere to belong. And physical activity is a critical part of that broader effort.”

The CHALK/Just Move program, which was started with a grant from the New York State Department of Health, has shown that bringing physical activity programs into schools can be simple, fun, and effective. CHALK is a classroom-based movement program in which classroom teachers follow the cues on a set of activity cards to lead kids in aerobic, yoga, stretching, and meditation exercises, getting them active right at their desks. Exercises are tied to the Common Core State Standards, allowing teachers to weave in math, science, and English language arts material to complement the day’s lesson plan. “Many schools add music to increase the fun factor,” says pediatrician Dodi D. Meyer, MD, Medical Director of CHALK/Just Move and Associate Professor of Pediatrics at Columbia University College of Physicians and Surgeons. “Pop music helps raise heart rates during vigorous exercises, while meditative tracks calm students at the close of each break, ensuring a smooth transition back to academics.”

Dr. Meyer points out that the New York City school system emphasizes the importance of good nutrition, but that there is less emphasis on physical activity. “Mrs. Obama’s new campaign is a way of raising awareness of the importance of physical activity in the school setting and raising accountability there,” she says. “A lot of schools in our neighborhood don’t have a licensed physical education teacher. A lot of schools don’t have gyms. A lot of schools don’t have outdoor play spaces.” Developed in an urban area with limited recreational space, the CHALK/Just Move program demonstrates that even in schools without a gymnasium or outdoor play space kids can become active, says Dr. Meyer. “The idea is to slowly start changing the culture of the nation, giving priority to healthy nutrition and promoting physical activity.”

ChildObesity180, a national organization of public, nonprofit, academic, and private-sector leaders committed to working together to reverse the trend of childhood obesity, and its Active Schools Acceleration Project (ASAP) have united with the First Lady on this new campaign. ASAP is awarding Acceleration Grants totaling $1 million to 1,000 schools to implement innovative physical activity programs, including CHALK/Just Move, to get kids moving.

The grants will provide the schools with the resources they need—seed funding, training, and support—to replicate the CHALK/Just Move or another school-based physical activity program. “This grant opportunity will help make physical activity an integral, welcome part of the daily lives of children across the country,” adds Dr. Meyer.

Teachers value the CHALK/Just Move program both as a transition tool to move students between subjects and as a reset button to help focus the class. The teachers have significant flexibility in implementing the program during the school day to best fit their lesson plan, making CHALK/Just Move practical for use throughout the school year and for a variety of schedule configurations.

According to Dr. Meyer, student ownership helps ensure that the program is fun and is embraced by the children, who vote on the songs they would like to hear, serve as the demonstration models on the activity cards, and help teachers run the breaks. Students in younger grades can demonstrate alongside their teacher, while those in older grades can become student leaders. By allowing students to guide their peers, CHALK/Just Move doubles as an exercise in confidence building.

“Research shows that physically active kids do better academically and behaviorally, and schools are a great place for boosting their physical activity,” says Steven J. Corwin, MD, Chief Executive Officer of NewYork-Presbyterian. “We’re delighted that the CHALK program has been selected as a promising approach to increase children’s physical activity and reduce the growing obesity epidemic in our nation. Fostering good health and well-being is an integral part of our patient care and community service mission as an academic medical center.”
Babies Hospital Alumni Day

Members of the Babies Hospital Alumni Association gathered for the 75th Annual Babies Hospital Alumni Day on April 26. The Alumni Association, which was established in 1938, welcomes as members faculty and doctors who have done a residency or fellowship at Babies Hospital (now the NewYork-Presbyterian Morgan Stanley Children’s Hospital). The Association’s goals are: “the advancement of the interests of Babies Hospital, the advancement of Pediatric art and science, and the promotion of social activities among its members,” according to its original by-laws.

This year’s meeting met all three objectives. The day began with three lectures: two by Infectious Diseases faculty Philip LaRussa, MD and Lisa Saiman, MD, MPH; the third was given by former resident, chief resident, and faculty Anupam Kharbanda, MD, MSC, who is currently Research Director of Emergency Services at Children’s Hospitals and Clinics of Minnesota. Dr. LaRussa spoke about “Vaccine Safety Issues in the 21st Century,” while Dr. Saiman spoke about “Experiences with Influenza: 2012-2013.” Dr. Kharbanda lectured on “Recent Developments in the Evaluation of Acute Abdominal Pain.”

Martin Blaser, MD, Professor of Microbiology and Director of the Human Microbiome Program at NYU School of Medicine, gave the 35th Annual Hattie Alexander Lecture on “Perturbing the Early Life Microbiome and its Consequences.”

John M. Driscoll Jr. MD, Reuben S. Carpentier Professor Emeritus and former Chairman of the Department of Pediatrics from 1992-2007, received the Babies Hospital Distinguished Alumni Award.

The lectures and awards ceremony were followed by lunch and a business meeting at which several additional awards were presented to current fellows, residents, and medical students (see Honor and Awards). To view the program and photos from the event, please visit the webpage at http://www.cumc.columbia.edu/pediatrics/about-us/alumni-association/alumni-day-2013.
In the News

**REUTERS**

Genes Should Not Be Patentable, Dr. Chung Asserts

The US Supreme Court is now weighing arguments in a case that questions whether human DNA can be claimed as intellectual property and remain off-limits to anyone who does not have permission from the patent holder. The case challenges the validity of gene patents, specifically those owned or controlled by Myriad Genetics, whose BRACAnalysis product detects certain mutations in the BRCA1 and BRCA2 genes; women with these mutations are at high risk for breast and ovarian cancer. In a recent Reuters article pediatrician and geneticist Wendy Chung, MD, the first plaintiff in the case, cites the example of three sisters whose DNA was analyzed for BRCA by Myriad several years ago. The sisters were found to have a “variant of unknown significance,” and elected to have prophylactic mastectomies in case the mutation was cancer-causing. The women were very unhappy when, years later, Myriad re-classified the variant as innocuous. “I think we could have moved a lot faster if the country’s scientific brainpower could have analyzed the patients’ BRC rather than rely on Myriad,” Dr. Chung told Reuters. Independent scientists could have studied not only whether the variant is dangerous or benign but also whether that risk is modified by the presence of other genes—crucial information when a woman is agonizing over whether to have her breasts removed, she said.

http://www.reuters.com/article/2013/04/14/us-usa-court-dna-idUSBRE93D08Q20130414

**THE NEW YORK TIMES**

Dr. Westhoff Questions The Use Of Routine Pelvic Exams

American women are typically given a pelvic exam during their routine gynecologic visits, whether or not they have symptoms or concerns that might warrant one. In a recent article in The New York Times blog “Well,” gynecologist Carolyn L. Westhoff, MD counted herself among the growing number of experts who say that, for women who are well, a routine bimanual exam is not supported by medical evidence, increases the costs of medical care and discourages some women, especially adolescents, from seeking needed care. Moreover, pelvic exams sometimes reveal conditions that lead to follow-up procedures—including surgery—that do not improve a woman’s health but instead cause anxiety, lost time from work, potential complications, and unnecessary costs, and in almost every case the condition is found to be benign. Dr. Westhoff said, “I’m an American gynecologist, and that’s how we were trained. It took many years for me to ask, ‘Why are we doing this?’”


**WNBC-TV**

It’s Safe For Young Teens To Take The Morning After Pill, Says Dr. Santelli

Brooklyn Federal Judge Edward Korman recently ruled that the so-called “morning-after pill” should be universally available—over the counter, and without a prescription to girls, regardless of their age. His ruling overturned a decision by Health and Human Services Secretary Kathleen Sebelius, who determined that girls 16 and younger should only be able to access the pill, which helps prevent pregnancy after sexual intercourse, with a doctor’s prescription. Commenting on the availability of the controversial emergency contraceptive sold over the counter as Plan B, pediatrician and adolescent medicine specialist John Santelli, MD told WNBC-TV that there is little likelihood of very young girls buying the pills. “The age groups in which it would be used, girls aged 13 on up, are pretty much able to understand instructions and it’s safe for them to take,” he said.

In the News

SCIENCE DAILY
Fish Oil May Protect Infants From Brain Damage Following Stroke, Dr. Deckelbaum Says

Stroke is more likely to occur in the perinatal period than at other times in childhood, and is associated with significant long-term neurologic impairment including mental retardation, cerebral palsy, and behavioral disorders. An article in Science Daily highlights research showing that a component of fish oil reduced brain trauma in newborn mice. The study, whose senior author is Richard Deckelbaum, MD, director of the Institute of Human Nutrition, showed that neonatal brain damage decreased by about 50% when a triglyceride lipid emulsion containing docosahexaenoic acid (DHA) was injected within two hours of the onset of ischemic stroke. Omega-3 fatty acids may have potential as neuroprotectants because they affect multiple biochemical processes in the brain that are disturbed by stroke, Dr. Deckelbaum said.

http://www.sciencedaily.com/releases/2013/02/130220184943.htm

THE NEW YORK TIMES
Drs. Phinizy And Hum Solve The Mystery Of The Baby Who Refused To Eat

A three-month old baby girl who had stopped eating was transferred to CUMC after two days in another hospital. Her case, and the fast-thinking doctors who solved it, appeared recently in The New York Times monthly feature, “Think Like a Doctor.” Pelton Phinizy, MD, the third-year pediatric resident on call when she arrived by ambulance, noticed her drooping eyelids, limpness, and a quiet gurgle in the back of her throat. “As soon as I saw her, I knew there was something wrong,” Dr. Phinizy told The New York Times. “All my alarms were going off.” Dr. Phinizy tracked down Stanley Hum, MD, the pediatric intensivist on call in the ICU that day. Dr. Hum was particularly intrigued by the suddenness of the paralysis in an otherwise healthy child. Only a few diseases could cause this, including Guillain-Barré, which would have shown up in the spinal fluid, he reasoned. Even without seeing the baby, and having only encountered the disease once before, Dr. Hum recognized a classic presentation of infant botulism. He ordered the botulism anti-toxin, BIG-IV, from its producer in California. It arrived the next day, and after a three-week stay in the ICU the baby returned home, back to her usual happy, hungry self.

https://www.youtube.com/watch?v=pcpPU5kyr30

REUTERS HEALTH
Dr. Wright Advocates More Research On Long-Term Outcomes From Minimally-Invasive Surgery

Minimally-invasive forms of heart surgery and fibroid removal may be less expensive and allow patients to take fewer days off from work than traditional, open versions of the same procedures, according to a study in JAMA Surgery. “From a patient’s perspective, whenever you undergo a surgery, you want to get back to your normal life and normal function as fast as you can,” gynecologic surgeon Jason Wright, MD told Reuters Health. Dr. Wright, who was not involved in the study, added that more research is needed on the long-term outcomes of many types of minimally-invasive surgery. And those outcomes may not look the same for every person. “It’s really important for patients, whenever they have a surgery, to sit down and talk with their doctors...about the efficacy of the procedure,” said Dr. Wright. “Each one of these really needs to be individualized,” he said. “Patients really need to be aware of their options.”

http://www.reuters.com/article/2013/03/20/us-surgery-cost-idUSBRE92J18M20130320
Linda Addonizio, MD, Director of the Pediatric Cardiac Transplant Program, was asked to be an instructor at the International Society for Heart and Lung Transplantation Master Academy: Core Competencies in Pediatric Heart and Lung Transplantation at the Society’s 2013 meeting in Montreal.

Mary E. D’Alton, MD, Professor and Chair of Obstetrics and Gynecology, received the National Institute of Ireland (NUI) Galway Alumni Award for Medicine, Nursing and Health Sciences. The award celebrates alumni around the globe who have made new discoveries; forged new industries andenterprises; and shaped Irish culture.

Brett Anderson, MD, Fellow in Pediatric Cardiology, received The Andrew King Research Award from Colín’s Kids Foundation.

Anne Armstrong-Cohen, MD, Assistant Professor of Pediatrics, has been selected as CUMC’s nominee for the 2013 Arnold P. Gold Foundation’s “Humanism in Medicine Award, which honors caring and compassionate faculty members who mentor medical students. Each medical school can nominate one faculty physician for this award; the nominee is chosen by the medical students.

Pediatric critical care specialists Scott Baird, MD, and Ravi Thyyar, MD, are collaborating with Donna Farber, PhD, a member of the Center for Translational Immunology, on her recently received NIH R01 grant to examine the development of lung T-cell responses in infant respiratory immunity. Drs. Baird and Thyyar will perform the patient studies for the research project in CUMC’s pediatric intensive care unit.

Erika Berman Rosenzweig, MD, Director of the Pulmonary Hypertension Comprehensive Care Center, received NIH funding as a co-investigator for a National Biological Sample and Data Repository for Pulmonary Arterial Hypertension (PAH). Dr. Berman Rosenzweig was also re-appointed as Pediatric Committee Chairperson for the Pulmonary Hypertension Association’s (PHA) Online University and Scientific Leadership Council.

Critical care specialists Katherine Biagas, MD, Associate Professor of Pediatrics, and George Hardart, MD, Associate Professor of Pediatrics and Bioethics, were both awarded Presidential Citations for Service by the Society of Critical Care Medicine.

Marina Catalozzi, MD, Assistant Professor of Pediatrics in the Division of Child and Adolescent Medicine, is the recipient of the 2013 Malim School Junior Faculty Teaching Award. This honor is presented by students to an assistant professor who is making an outstanding contribution to education.

Jessica Fanzo, PhD, newly-arrived Assistant Professor in the Division of Gastroenterology, Hepatology and Nutrition and the Institute of Human Nutrition, received the 2012 Premio Daniel Carasso Prize from the Daniel and Nina Carasso Foundation for her outstanding work on sustainable food and diets for long-term human health. Dr. Fanzo’s work has focused on “food system” approaches to improved food security and nutrition for vulnerable populations in sub-Saharan Africa and South Asia.

David A. Gass, MD, Hem/Onc Stem Cell Fellow, was awarded the Metropolitan Fund Fellowship. This award is presented annually to a fellow demonstrating excellence in hematology, oncology, and stem cell transplantation.

Anne Gershon, MD, Professor of Pediatrics and Chief of the Division of Pediatric Infectious Diseases, was selected to receive the Gold Medal of the Albert Sabin Vaccine Institute for 2013 for her research on variella zoster virus (VZV) and VZV vaccines against chickenpox and shingles. Dr. Gershon was also invited to deliver the Stanley Plotkin, MD, annual lecture in vaccinology at the 2013 Pediatric Academic Societies meeting in Washington, DC.

Thomas Hooven, MD Neonatology Fellow, received The Milton Singer Memorial Fellowship, which is presented annually to a talented physician who is planning a research career focused on cerebral palsy or prematurity.

Colleen Kays, P&S medical student, is this year’s recipient of The William Perry Watson Prize, which is awarded to the graduating medical student who shows “the most valuable work in the study of the diseases of infants and children during his or her regular courses.” The prize was established in 1922 by a gift from Dr. Watson, who graduated from P&S in 1878.

David Kessler, MD, MSc, RDMS, Assistant Professor of Pediatrics in the Division of Emergency Medicine, was invited to teach a pre-conference workshop entitled, “Teaching Procedural Skills using Simulation” at the 2013 International Meeting on Simulation in Healthcare. Dr. Kessler also gave a presentation entitled, “Building Capacity for Multi-center Simulation Research: Strategies for Success in Developing an International Specialty Specific Simulation Research Network.” Dr. Kessler was a faculty member at the 2013 annual regional BASE Camp, an immersive simulation-based teamwork and skills training educational experience for pediatric emergency medicine fellows in northeastern US.

Esi Lamoue-Smith, MD, PhD, newly recruited from Harvard/Boston Children’s to the Division of Gastroenterology, Hepatology and Nutrition, was the first recipient of a Diversity Supplement from the Provost and Dean of Medicine to begin her research at Columbia in the Center for Translational Immunology. She will be investigating the role of the gut microbiome in adaptive immunity in response to viral infections and vaccinations.

Teresa Lee, MD, Fellow in Pediatric Cardiology, received The Andrew King Research Award from Colin’s Kids Foundation.

Sruti Nadimpalli, MD, Fellow in Pediatric Infectious Diseases, has received an Early Career Award from the Thrasher Research Foundation for her project entitled, “Identification of Infectious Agents in Bronchoalveolar Lavage Specimens Using New Diagnostic Methods.”

Richard A. Polin, MD, Professor of Pediatrics, Vice Chair, and Chief of the Division of Neonatology, has been appointed Chair of the Neonatal-Perinatal Medicine Sub-board of the American Board of Pediatrics.

Marc Richmond, MD, Assistant Professor of Pediatrics in the Division of Pediatric Cardiology, received The Colin Molloy Research Award from Colin’s Kids Foundation.

David Sparling, MD, PhD, Endocrine Fellow, was awarded this year’s Rustin McIntosh Fellowship, which honors a fellow with a “spirit of doubt and need for inquiry,” qualities Dr. McIntosh exemplified during his tenure as Chairman of Pediatrics and Director of the Pediatric Service from 1933-1960.

Daniel Stephens, MD, third-year resident, received this year’s Edward C. Curnen, Jr. Award, established by Dr. Curnen’s colleagues to honor the house officer who cares for patients with the kind of humanity and compassion that Dr. Curnen displayed during his long and distinguished career in pediatrics.

The Flu Text Influenza Text Messaging program developed by Melissa Stockwell, MD, MPH, Assistant Professor of Pediatrics and Population & Family Health, and her research group was selected by the RAND Corporation’s Promising Practice Network as a practice “proven” to improve outcomes for children (the highest evidence level). Dr. Stockwell also received an “Honorable Mention” in a special edition of News Digest, “Who’s Who in Academia,” which recognized faculty who are making a difference at institutions of higher education.

The International Society for Heart and Lung Transplantation accepted five abstracts from the faculty of the Program for Pediatric Cardiomyopathy, Heart Failure and Transplantation for presentation at the Society’s 2013 Meeting. The abstracts were:

Richmond ME, Kimberly Beddows, et al. “Elevated Pre-Transplant Pulmonary Vascular Resistance is Not Associated with Mortality in Children without Congenital Heart Disease: A Multi-Center Study.”


Hahn E, Zuckerman WA, Richmond ME, Chen JM, Singh RK, Addonizio LJ. “A Novel Echocardiographic Measurement in Pediatric Heart Transplant Recipients With Dilated Cardiomyopathy: Can We Maximize the Donor Supply?”

Ramey J, Stare T, Zuckerman WA, Addonizio LJ, Richmond ME. “Incidence and Importance of New Post-Operative Right Bundle Branch Block After Pediatric Orthotopic Heart Transplantation.”

Rakesh K. Singh, MD, MSc, Warren A. Zuckerman, MDa, Marc E. Richmond, MD, MSc, Teresa M. Lee, MDa, Kimberly D. Beddows, CPNPa, Lisa A. Gilmore, CPNPb, Jonathan M. Chen, MDs, and Linda J. Addonizio, MDa, “HeartMate II® Left Ventricular Assist Device Placement in an Adolescent Duchenne Muscular Dystrophy Patient with Severe Dilated Cardiomyopathy.”
At the 15th Annual Pediatric Fellows Poster Day Presentation on May 23, three fellows were awarded the inaugural Sharon Oberfield, MD, prize. Each of the awardees presented their research while all of the 22 abstracts submitted for consideration were on view in the Wintergarden. The three winning posters are summarized below.

The winning poster in the translational research category was entitled “Longitudinal Microbial Ecology in Cystic Fibrosis.” Second-year pulmonary fellow Gina Coscia, MD, presented the research, which looked at how specific changes in microbial diversity in the lungs of patients with cystic fibrosis (CF) correlate with changes in clinical status. Among the 154 patients in the study the researchers found that there may be an equilibrium baseline community in CF that is significantly perturbed during pulmonary exacerbations as well as a correlation between lung function and overall microbial diversity.

In the basic research category, the winning abstract was entitled, “The Role of Notch in Adipose Tissue.” Second-year fellow David P. Sparling, MD, PhD presented the study, which looked at Notch, a paracrine signaling receptor associated with cell-fate decisions as well as with metabolism regulation in liver and skeletal muscle. Dr. Sparling and his colleagues hypothesized that the Notch signaling cascade is both present in and regulates the various adipose depots in multiple metabolic states. Their findings suggest that Notch is active in and can regulate adipose tissue function in vivo, with effects on whole body metabolism.

Third-year fellow Brett R. Anderson, MD, MBA presented the winning abstract in the clinical research category, “A Prompt Arterial Switch Operation Improves Outcomes and Reduces Costs for Neonates With Transposition of the Great Arteries.” The research group examined the impact of timing of arterial switch operation (ASO), the standard of care for neonates with dextrotransposition of the great arteries. They examined factors including major morbidity or mortality and hospital reimbursement for late preterm and term infants with uncomplicated transposition of the great arteries (TGA). Their findings suggest that delay in surgical correction of simple TGA in late preterm and term infants is associated with a significant increase in both morbidity and healthcare costs.

Erin Qualter, MD
Before entering medical school Dr. Qualter was a pediatric oncology/blood and marrow transplantation research nurse practitioner at Morgan Stanley Children’s Hospital. During that time she produced a number of publications and presentations. Dr. Qualter attended Albany Medical School, where she was inducted into AOA and the Gold Humanism Society; she graduated cum laude. Now a third-year pediatric resident, Dr. Qualter will be pursuing a fellowship in neonatology at Mt. Sinai Hospital. During her residency she completed a research project, “Incidence and risk factors for pneumothorax in extremely low birth weight infants during the first week of life.” Dr. David A. Bateman was Dr. Qualter’s research mentor for this project. She has submitted an abstract to Pediatric Academic Societies and is currently in the process of writing the manuscript for this study.

Sarah Richman, MD, PhD
Dr. Richman is a third-year pediatric resident who will continue her training in pediatric hematology/oncology at the Children’s Hospital of Philadelphia. Dr. Richman attended the University of Illinois, graduating AOA with an MD/PhD in biochemistry. She has been involved in research in the lab of Megan Sykes, MD, investigating neutropenia and T-cell chimerism after solid organ transplant. Dr. Richman plans on pursuing a career as a physician-scientist with research as an integral part of her work.
families. At the same time they are in touch with other geneticists around the world who have similar patients, so that they can create a clearer picture of what these diagnoses mean for the future of these newborns.

For patients and their families it can be somewhat terrifying to be diagnosed with a brand new disorder: the future is uncharted and treatments unknown. “It’s an interesting journey for these families who are literally at the forefront of biomedical research,” Dr. Chung says. “It’s like they’re in the wilderness and wandering for a little while until we start getting enough data to know what these diseases entail while identifying larger numbers of patients.” Often patients who come for clinical care end up participating in research studies, says Dr. Chung, “and work with us to push this frontier forward. And this interface between the clinical work and the research is what we’re good at.”

Drs. Chung and Wapner come to genetics from complementary angles: Dr. Wapner is Director of Reproductive Genetics and Vice Chairman for Research in the Department of Obstetrics and Gynecology, while Dr. Chung is Director of Clinical Genetics in Pediatrics and treats children who either arrive in the world with a birth defect or have problems as they develop and grow. Both are testing the limits of powerful new genomic technologies, moving them from research to the clinic, and using them to diagnose disorders in fetuses and children. “Our tools are dramatically changing, and that’s where the rubber meets the road, so to speak,” Dr. Wapner says. As lead investigator of the National Institutes of Health sponsored clinical trial of 4,400 women who underwent a new form of molecular diagnostic testing called chromosomal microarray analysis (CMA), he demonstrated that CMA identifies more problems than the longstanding test, karyotyping.

Dr. Wapner’s collaboration with Dr. Chung spans the pre- and postnatal sides of the CMA research study, as she continues to follow 200 children whose genetic abnormalities were uncovered during the study over the next three to five years. With the information she gathers, he says, “we’ll be able to get a better picture for future parents: what these genetic deletions or duplications mean and which interventions could make a difference. Most importantly, we will be able to introduce interventions way earlier than we would without this knowledge.”

While microarray analysis yields information about diseases that arise from small missing or extra pieces of DNA on chromosomes, in sequencing geneticists examine every base pair along a strand of DNA and find diseases linked to changes in a single genetic letter. “These seemingly minute changes can alter the production of specific proteins and give rise to diseases like sickle cell disease,” Dr. Wapner says. “Because they identify different genetic abnormalities and different diseases, the two tests complement each other,” he adds. “These two tests have, in some sense, developed in parallel with each other, and the question now is how we can combine both together.”

Sequencing technology lags behind CMA by a couple years, and is currently slower and more costly. While a CMA analysis can be completed in 5 to 10 days, sequencing results take 5 to 10 months. Dr. Wapner is developing techniques to speed the results of sequencing, so that they will be useful for evaluating a particular pregnancy. “We can’t look at every piece of DNA if we have to get the results in three weeks,” he says. “Instead we will have to gather a lot of information about what genes cause specific birth defects. If we know that, say, birth defect A is likely to involve specific genes, we can then do more targeted sequencing.”

The stakes are tremendously high if a genetic abnormality is discovered in utero, when parents may decide, based on the test results, to terminate a pregnancy, so Drs. Chung and Wapner strive to understand the postnatal implications of new genetic technologies before offering them to prospective parents. “As partners, Ron and I figure out at least some of the complexity on the postnatal side where the information is critically important but where you’re not dealing with the same kind of uncertainty,” says Dr. Chung. When there’s not enough information to advise couples fully on the implications of a detected abnormality, “we try to help them think through where they are in their lives at that moment and what they can handle,” she says. “Some couples take it in stride while others are tormented by not knowing with certainty what the problem is or how severe it’s going to be, so testing is not for everyone.”

An advantage for parents who do decide to continue a pregnancy is that they can receive care in the Center for Prenatal Pediatrics and deliver at the NewYork-Presbyterian Morgan Stanley Children’s Hospital, where their newborn will get the care and evaluation he or she needs, Dr. Chung says. Newborns known to have a genetic disease will be carefully monitored for potential problems. “As they grow up, many children with genetic disorders have both special medical and educational needs,” she says. “We can often prognosticate for parents exactly what those needs are going to be, and can help them avoid future medical problems because we’ve anticipated correctly what the child will be at risk for.”

CUMC’s Center for Prenatal Pediatrics, neonatal intensive care unit, and the partnership among maternal-fetal medicine specialists, pathologists, genetic counselors, pediatricians, fetal cardiologists, and other specialists who all work together, have made CUMC a major referral center for genetic problems both pre- and postnatally, Dr. Wapner says. Dr. Chung adds, “Ron and I and all of the other practitioners we work with really coordinate the services for fetuses at high risk between maternal-fetal medicine to pediatric subspecialists. We really offer the whole package.”

— Beth Hanson
Beyond Antibiotics CONTINUED FROM PAGE 1

Dr. Prince, an infectious disease specialist with appointments in the Departments of Pharmacology and Pediatrics, is investigating the complicated interplay between bacteria and their hosts. She realized very early in her research career that the host’s response was central to the pathogenesis of infection, she says, and that diseases caused by bacteria occur usually when the host produces an excessive response or inflammation to the organisms. “If you didn’t look at the host you couldn’t really understand how the bacteria and the host were interacting,” she says.

Dr. Prince initially focused her research on children with cystic fibrosis (CF). The mutation that causes CF affects the immune response to bacteria, causing children with the disease to have a hyper-immune response to bacteria in their airways, she says. “Organisms that you and I inhale every day, we just clear and nothing happens.” When children with CF become infected, the organisms gradually adapt to the conditions within the lung. “These kids develop a smoldering inflammation that gets worse and better, worse and better, and it’s the inflammatory response to the organism that eventually ruins their lungs,” Dr. Prince says. Over time her research has broadened beyond CF to the range of host responses to bacteria, with a focus on *Pseudomonas aeruginosa* and *S. aureus*.

Both of these bacteria often enter the body when they are inhaled into the airway. There they encounter the airway epithelium, a layer of tissue that includes both physical barriers and the complex array of receptors that constitutes the innate immune system. Once activated, this system initiates the production of signaling molecules (proinflammatory cytokines), antimicrobial proteins, and the recruitment of immune cells to the site of infection. Dr. Prince probes the interactions among the different components of the immune system using mouse models. “In mice you can knock out specific immune responses and ask, what does the mouse need to clear pneumonia? Do you need antibodies, T cells, macrophages, polymorphonuclear leukocytes? Is any one component critical?”

Over the course of her career, and through a number of studies, Dr. Prince and colleagues have shown that, “there’s so much redundancy in innate immune signaling that actually knocking out different cell types or different inflammatory pathways can improve the host and make it better.” In a recent paper, for example, Prince and lab member post-doctoral fellow Taylor Cohen, PhD examined host response to *P. aeruginosa*, which is a major cause of ventilator-associated pneumonia. (Cohen TS, Prince AS, J Activation of inflammasome signaling mediates pathology of acute *P. aeruginosa* pneumonia. J. Clin Invest. 2013 Apr 1;123(4);1630-7)

*P. aeruginosa* use appendages called flagella to propel themselves toward carbon sources, and these flagella excite an immune response in the host cells; this response is mediated by the inflammasome, a group of receptors that recognize molecular patterns expressed by invading pathogens. When activated, the inflammasome initiates production of pro-inflammatory cytokines (especially IL-1β and IL-18). Drs. Prince and Cohen showed that when inflammasome signaling was induced among mice with acute pneumonia, they were less able to clear the bacteria, and mortality rates were higher. The researchers explored a number of strategies to limit inflammasome activation (infection by fliC mutants, depletion of macrophages, deletion of NLRC4, reduction of IL-1 and IL-18 production, inhibition of caspase-1, and inhibition of downstream signaling in IL-1R- or IL-18R-null mice), and showed that all of these strategies resulted in enhanced bacterial clearance and diminished levels of disease. Their study showed that treatment approaches that target the inflammasome have the potential to limit the consequences of acute *P. aeruginosa* pneumonia.