



CLINIC FOR SPECIAL CHILDREN NEWSLETTER

VOLUME I NUMBER 31

* LANCASTER COUNTY, PENNSYLVANIA *

SUMMER 2011

From the outside looking in, the Clinic seems like a simple place. Our basic mission is, in fact, simple. We are here to provide special help for those who need it, one child at a time. And yet, doing this well requires efforts by many people on many different fronts. As any caregiver knows, there is always more that can be done and no one person can do it all. We are reminded daily of the challenges that special children and their families face. As long as such needs remain, we all have important work to do.

As we recognize new problems within the community, our sphere of concern grows: we see local children who have medical problems never before encountered and also see familiar problems in children who come from far away. Both types of issues compel us to act but they require different kinds of solutions. How will we help this child afflicted with a new and complex form of brain disease? How can we protect this family from crushing medical bills? How can we help the many special children who live in Kentucky, New York, North Carolina, Ohio, Indiana, and even farther away?

We try earnestly to address the needs before us each day but must also look to tomorrow. We know that special children, difficult problems, and the call to compassionate service will always be with us. To vouchsafe the future, education and outreach will play a vital role. Educating parents gives them comfort and hope; educating local midwives, physicians, and nurses makes our community stronger; educating colleagues around the world is our part in the commonweal; educating students is our gift to the future.

It would be impossible in this short space to describe all of the work that defines the Clinic today. Indeed, there are so many who work for us quietly, persistently, in ways that remain hidden from view: Board members, office staff, the auction committee, parents, grandparents, deacons, bishops, hospital staff, midwives, scientists, teachers, students, and volunteers. All are integral to the Clinic family, and are testament to the fact that this is not, and has never been, the work of one or a few. It is especially for them that we highlight in this issue of the Newsletter just some of the progress over recent months, so that all can understand how much we value their efforts.

Kevin Strauss, M.D.

*Time is that wherein
there is opportunity, and
opportunity is that
wherein there is no great
time. . . . Healing is a matter
of time, but it is also a matter
of opportunity.*

—Hippocrates, Epidemics



We are very grateful for the support received from last year's benefit auctions. Together, the four events brought a record level of funding for the clinic's annual operating budget. We hope to have enthusiastic support again this year at all of the auctions. As we often say, benefit auctions are a lot more fun than writing grants - and possibly much more productive!

BENEFIT AUCTION DATES FOR 2011

July 9, Shiloh, Ohio

July 16, Shippensburg, PA

September 10, Blair County, PA

September 17, Lancaster County, PA

Families in **Shiloh, Ohio** will again sponsor an auction to benefit the clinic on **July 9th** at the Blooming Grove Auction Center, located at 1091 Free Road, Shiloh, OH. This event supports both the Clinic for Special Children and the DDC clinic in Middlefield, OH. We are very grateful for the support growing from this community.

Ice cream always sells on a hot July day to a crowd in **Shippensburg**. In addition to quilts and wall hangings, new wagons and furniture, this auction always has many garden items and beautiful plants donated for sale on **July 16th** at the Shippensburg Auction Center on 1120 Ritner Highway, (Rt. #11, 1 mile north of Shippensburg). Remarks by Dr. Morton are scheduled for 11:45 a.m. with the quilt sale at noon. Sale Committee contacts for information or donations are: Elvin Oberholtzer, Chairman, 99 Koser Lane, Shippensburg, PA 17257, 717 532-9088; David Zimmerman, Treasurer, 717 532-5221; and David Leinbach, 717 532-3642.

The annual auction in **Blair County** is on **September 10th** at Morrison's Cove Produce Auction on Rt. 36, south of Roaring Spring, PA. In addition to many beautiful quilts, furniture, chicken barbecue and soft pretzels, plants and especially mums for fall bring in bidders from the central Pennsylvania region. Contact: 814-224-5442; 814-793-3010.

As always, the last auction of the year is in **Lancaster County** on the third Saturday of September, this year, **September 17th**, at the Leola Produce Auction on Brethren Church Road (north from Rt. 23) in Leola. The auction begins at 8:30 am, but breakfast is available from early morning. Dr. Morton and Dr. Strauss will speak at 11:00 a.m. with quilt and furniture sales following at 11:30. This will be the 21st year for the auction, planned by the same group of volunteers who planned the very first auction for the Clinic in 1991. We are very thankful for their faithful and enthusiastic support....and for their attention to all the details that make the auction successful year after year.

FROM LAST YEAR ~ Who was there and what did we have to eat? It was a record auction in many ways. There were 1542 buyer's numbers signed out with many duplicate cards provided for family members to use for bidding. Nineteen auctioneers and eleven clerks volunteered. Approximately 3,936 items, all donated, were sold at seven simultaneous auction blocks, four inside and three outside between 8:30 am and 5:45 pm when the gavel sounded after the last item was sold. Quilts are always a feature of the sale and last year there were 79 large quilts and as many smaller, wall hanging sizes. Most of the large quilts were made especially for the Clinic's auction by friends and family members of children who receive services at the Clinic. Other featured items included many pieces of handmade furniture, original art work, a unique marble roller, a new Amish carriage, a pony with harness and wagon, a hand carved wooden chest, garden furniture and sheds.

*From A Sampling of 2010,
A Preview for 2011:*

2300 Subs
15,000 Donuts
4000 Soft Pretzels
110 gallons of Lemonade
Ham & Cheese Sandwiches
288 Waffles & Ice Cream
3000 pounds of Barbecued Chicken
3700 pounds of Potatoes for French Fries & Chips
Fried Pies, Fruit Pies, Salad Bar, Fruit Cups
4000 Whoopie Pies in 8 variations
500 gallons of Ice Cream
500 Smoothies
600 Pancakes
700 Omelets
720 Pizzas
8 Roasted Pigs

***THANK YOU** to all who volunteer; to all who donate sale items and prepare food; to all who attend; to all who bid; to all who enjoy the food. Most importantly, we thank the children who inspire all of us to keep the Clinic growing and thriving as a source for their comfort and care.*

ANNUAL MATCHING CHALLENGE

We are very grateful to a Lancaster area foundation for their annual matching challenge of \$50,000. Last year we met the match by the deadline with the help of 82 donors. This year we are challenged to meet the matching amount of \$50,000 by December 1st. AND we seek this year **TO DOUBLE THE MATCH!**

PLEASE HELP DOUBLE THE 2011 MATCH and send contributions to The Clinic for Special Children, P.O. Box 128, Strasburg, PA 17579.

We thank all who contribute to this challenge fund and especially the generous foundation which provides the matching fund.



Postage Stamp Wall Hanging

The Postage Stamp Quilt is a very special quilt each year. It has been made by the same person for the last 16 years for our auction as a gift. Each year she sews 5,103 one inch patches together and quilts around each square. Over the last 16 years the sale of postage stamp quilts has given a total of \$28,000 to help the Clinic care for special children. We are grateful!

Clinic Model Workshop

We are often asked if the Clinic for Special Children is the only one of its kind? Could the model of our Clinic work in other places, serve other communities? How would such a clinic be established and supported? We have some ideas and we are also hopeful as other clinics serving special needs children in other places are established and growing. The Das Deutch Center (DDC) in Middlefield, Ohio has been in operation for ten years and completed a beautiful new facility last year. The inspiration generated by a few families who visited our Clinic many years ago was translated into a thriving clinic serving the needs of many children in the Geauga County region of Ohio. In central Indiana, the Community Health Center (CHC) is ready to open after several years of planning and local community effort.

In late March, more than 60 participants gathered at The Clinic for Special Children for a day to study the characteristics involved in effectively planning, building, and operating clinics for children with special needs. Workshop participants came from Indiana, Ohio, and across Pennsylvania. Also attending were professors and students from Franklin & Marshall College, physicians, scientists, nurses, and staff from several different clinics, some with years of operation and others in the formative stages. Dr. Morton opened the workshop by reviewing the mission, principles, and goals, which have guided the work of the Clinic since he and Caroline founded it in 1989.

In human terms, the benefits of the Clinic for Special Children model are clear. Through early diagnosis and a system of comprehensive care, the work in these clinics can prevent problems like mental retardation, brain degeneration, lethal infection, and untimely death. Moreover, this clinical approach will allow study and increase understanding of the relationships among genes, environment, and disease. Improved understanding, combined with accessible, affordable and effective medical care, can often reduce suffering, improve function, reduce dependency on others and limit the effect of disease, genetic and acquired, on the life of a patient.

CSC Lab Director Dr. Eric Puffenberger reviewed the distribution of genetic disease in Plain Communities in North America and the role the CSC lab plays in diagnosis, treatment, and patient-determined research. Drs. Strauss and Morton led discussions on topics prompting the following statements and questions:

◆ Knowledge of genetics of Plain Communities leads to better local medical care for children and adults with special needs.

◆ How can the work of the Clinic for Special Children, Das Deutch Children's Clinic in Ohio, the Community Health Center in Indiana, be supported and sustained?

◆ What sources of support are available to help underwrite the start-up and sustaining costs of new clinics for special children that are under consideration in central PA, Holmes County, OH, and in other communities?

◆ Should clinics concentrate on delivering care only for "special" children with medical complications related to genetic disorders or can they serve all children in tandem with the specialized care required for children with complex needs?

◆ How do the economic models or business plans vary? It was noted that a clinic, which expects fees to cover all costs of care for special children, soon finds that families who self-insure cannot afford its services, or that when the fees are set at affordable levels, it cannot afford to attract and keep competent staff. DDC has been able to raise start-up, capital, and sustaining funds from foundation grants, which have allowed fees to be kept unusually low – clinic fees account for 4.5% of revenue, donations and grants 95.5%. CSC has operated using a model in which clinic fees typically account for less than 30% of revenue, community contributions through auctions add about 33%, and about 37% of income comes in the form of donations and grants and income from the education and research fund.

◆ Finding the "right" physician is a critical step. Dr. Morton found the children, recognized their needs, and was determined to treat them where they lived. He and Caroline were committed to establishing a clinic, and sought the help of community leaders to turn their vision into a reality. The organizers of DDC in Ohio searched for a physician for 3 years and hired Dr. Heng Wang 10 years ago as the Medical Director of DDC. Dr. Wang had read about the work at CSC and was interested in finding similar inspiring work. CHC (Indiana) has every thing in place to begin treating patients, and has just recently found a physician to direct the clinic.

Paul Morton, Dr. Morton's brother, is working on the comparison of clinic business models and funding sources. Please contact him at the Clinic for a copy of the clinic modeling plans.

Seeds Are Planted for A Clinic in Central Pennsylvania

Many families from central Pennsylvania (Somerset, Blair, Bedford, Centre, Huntingdon and Juniata Counties) now travel to Lancaster County to our Clinic to find the care their children need. The distance, time and travel expense involved present hardships for many. The Clinic for Special Children is working to help community leaders plan and establish a central Pennsylvania clinic to serve special children.

Dr. Greg Mock, a physician in the Martinsburg area is prepared to serve as the Medical Director of the new clinic. Dr. Mock and community leaders are seeking a local, active board of directors to work with them in developing the clinic which will be an independent organization but will work closely with the Clinic for Special Children.

Our special needs children have no choice and our ability to provide them with health care can make the difference of living a life of fulfillment or one of being trapped in a dysfunctional body or mind. Health care for the general community can be found easily, but health care for special needs children is very specialized and time consuming. The Clinic for Special Children in Strasburg has done the ground work for our communities in developing ways to keep these children healthy and identifying genetic problems which, left untreated, will have devastating results and, if treated appropriately, provide a way for these

individuals to have a healthy, full life in a body and mind that work normally.

As to an argument of which group of individuals are in the most desperate place for obtaining health care, there really is none. Special needs children obviously have the highest priority in that they cannot obtain appropriate health care at local health care centers or hospitals and tremendous sacrifice is made by these families to meet these needs. As we go along the pathway of developing the Central Pennsylvania Clinic for Special Children, my hope is that we can provide specialized health care locally for these children and save these families marked hardships which include long travel distance, high medical expenses and difficulties in obtaining daily support for special diets, testing or information needs. Truly these are a group of very special individuals who have arrived at their places in life not by choice and it is our responsibility to give them our best.

.....words from Dr. Greg Mock



PROGRESS ON MANY FRONTS

IMPROVED MEDICAL CARE : BETTER NUTRITION

We have teamed up with Applied Nutrition Corporation to provide better care for children with maple syrup urine disease (MSUD), glutaric aciduria type 1 (GA1), and other genetic conditions. A new formula, Complex Junior, has improved the metabolic control and overall health of children with MSUD while reducing their rate of hospitalizations by 60%. We recently completed testing for a new GA1 formula, Glutarade, over a 5-year trial. Fourteen consecutive children (29 aggregate patient-years) managed with Glutarade are free of brain injury. This represents a 36% lower risk of disability compared to 2005, and a 94% reduction of neurological risk since the Mortons established the Clinic in 1989. Glutarade will be available to children all over the world beginning July 2011. Its release will be accompanied by the publication of our treatment protocol in an international scientific journal. We are working on several other projects with Applied Nutrition: a formula for propionic acidemia, pre-packaged isoleucine, valine, and leucine for MSUD families, and a "ketogenic" formula for children with severe epilepsy, CNTNAP2 (CASPR2) disease and STRADA deficiency (Pretzel syndrome).

VISION AND HEARING LOSS are among the most serious chronic disabilities of children and adults worldwide. We can diagnose at least seven gene defects that threaten vision in young children: TUBGCP6 (Mennonite microcephaly), LAMB2 (Pierson syndrome), FLVCR1 (posterior column ataxia-retinitis pigmentosa), HARS (Usher-like syndrome), ADAMTS10 (Weill-Marchesani syndrome), LRP5 (OPPG syndrome), and AMN (hereditary B12 malabsorption).

In collaboration with pediatric ophthalmologists Drs. Lee Klombers and Brian Mohny, we now use a simple surgical technique called peripheral photocoagulation to preserve vision in children who have Pierson syndrome or Mennonite microcephaly. Dr. Alex Levin of the Wills Eye Institute has applied the technique of lens removal (lensectomy) to protect the eyesight of children with Weill-Marchesani syndrome. **We are grateful to Lancaster General Hospital for their donation of a \$16,500 hand-held retinal camera** that will improve our ability to study and manage genetic eye diseases.

Hearing loss, like blindness, can be tragic. Since installation of the Clinic hearing lab, we offer testing to an ever-increasing number of children. This service is linked to our effort to map the multiple genetic causes of hearing loss in Plain populations. Determining underlying causes improves our ability to screen couples at risk, individualize treatment, and in some cases prevent progressive hearing loss. We are grateful to Lynda Steelman, a board-certified audiologist, who provides state-of-the-art testing and management of hearing aids on site at a fraction of what these services cost elsewhere.

UNDERSTANDING DISEASES:

Severe Combined Immunodeficiency (SCID) is a dangerous condition that takes many forms in the Plain community (ADA, RAG1, IL7R, ARTEMIS). In June, seven families came to the Clinic to share their stories and hear Dr. Rider and experts from Philadelphia and Pittsburgh describe progress in the diagnosis and treatment of SCID. Topics included newborn screening, carrier testing, and bone marrow transplantation. The day concluded with evaluation of four children who were treated with bone marrow transplants, all of whom are currently healthy. Dr. Rider addressed some of the challenges that need to be overcome in the battle against SCID. These include laboratory work by Dr. Erik Puffenberger, Adam Heaps, and Anthony Weaver to expedite HLA patient-donor matching, rapid diagnosis of high-risk infants, carrier testing for young couples, and imperatives for doctors to get affected infants to the best transplant centers as quickly as possible and insure that their care is affordable.

Cartilage Hair Hypoplasia (CHH), another condition that threatens immune system function, continues to be a focus of study at the Clinic. Dr. Rider's collaboration with doctors from Children's Hospital of Boston and around the world led to a recent publication about CHH in the *Journal of Allergy and Clinical Immunology*. This manuscript details immune cell growth and function among people with CHH and has deepened our understanding of the condition. We hope these insights might ultimately improve care for affected children.

Our study about the long-term treatment of **pyruvate kinase deficiency (PKD)**, led by Dr. Rider, was recently accepted for publication. This work details the health risks and appropriate care of PKD patients from infancy to adulthood. It includes a 17-year history of PKD treatment at the Clinic, which began when Dr. Morton made the first correct diagnosis of an Amish infant in 1994. Since that time, treatment has steadily improved as a result of long, cumulative experience caring for children and a deeper appreciation for the problems that adults face. We are grateful for the help and advice from physicians around the country and from laboratory experts in Austria and England led by Dr. Heinz Zoller. We hope this paper will promote excellent care for PKD patients worldwide.

IMPROVING CARE THROUGH COLLABORATIONS:

We are indebted to the many specialists who dedicate themselves to our patients and can list only a few of them here. **Dr. Devyani Chowdhury** helps diagnose and manage Plain children with congeni-

tal heart malformations and cardiomyopathies (diseases of the heart muscle). Her compassion and expertise are invaluable to our mission. **Drs. Roy Small and Ron Jacob from the LGH Heart Group** enthusiastically donate their time and clinical skill to adults who have mutations in *ANT1* or *LMNA* that predispose to progressive heart damage. All three cardiologists see patients at the Clinic free of charge, and thanks to the reliable **Patrick Donnelly**, we continue to offer echocardiograms at the Clinic for less than \$200. For comparison, cardiology consultation at most referral centers costs about \$5000. Dr. Jacob has worked with administrators at Lancaster General Hospital to secure the donation of a new ultrasound-echocardiography machine for the Clinic and a gift of 10 free cardiac MRIs—a collective value of more than \$200,000.

Dr. Sander Markx, a psychiatrist and professor from Columbia University, returned in May for a day devoted to families struggling with serious mental health problems. He has launched two new gene mapping studies seeking genetic causes of bipolar illness in these families. Dr. Markx is also interested in the genetic basis of common and disabling problems like depression, schizophrenia, autism, and attention-deficit hyperactivity disorder—all of which occur among Plain communities - and he continues his research into treatment of *CNTNAP2* (*CASPR2*) deficiency. These are complicated projects that require careful thought and planning, but over time we hope to alleviate some of the deep suffering caused by mental illness.

Ongoing collaboration with **Dr. Gordon Baltuch**, from Pennsylvania Hospital has allowed us to offer some patients with movement disorders the cutting edge of treatment. Dr. Baltuch is a world leader in deep brain stimulation—the implantation of pacemakers in the brain to control involuntary muscle spasms and contractions. Two of our patients had this surgery in the last month and both report positive results. We expect many other patients with movement disorders can benefit from this innovative procedure.



Summertime in the Clinic parking lot

PROGRESS IN THE LABORATORY

GM3 synthase deficiency is a serious neurological disorder among the Amish caused by a mutation in *ST3GAL5*, an enzyme that produces molecules called gangliosides. Gangliosides are highly concentrated in the brain where they are essential for normal growth and function of nerve cells. GM3-deficient infants can develop seizures, blindness, and hearing loss, and their neurological development ceases at an early age. Most of these children are unable to sit up, walk, or speak. **Kert Ivie, Vice President of Scientific Systems, Inc. in State College, PA**, recently donated a new ultra-fast flow liquid chromatography (UFFLC) machine to help us develop a method for measuring gangliosides in blood and **Waters Corporation** kindly donated necessary lab supplies. This is the first crucial step toward our goal to develop a

treatment for GM3 deficiency. Friends of the Clinic are providing invaluable help: **Steve Roth, Franklin & Marshall chemistry professors Ryan Mehl and Ken Hess, their student Josh Wesalo, and especially Matt Kremer**, who keeps the project organized and moving forward.

About a year ago, the Clinic piloted a new diagnostic technology called exome sequencing in collaboration with the **Broad Institute** in Boston. Exome sequencing allows us to examine an individual's entire DNA code, all 25,000 genes, in a single test run for a cost of less than \$1000. We undertook the pilot study to determine if exome sequencing could be clinically useful and sent Broad DNA samples from 9 different conditions, all of which were studied for many years at the Clinic without finding an underlying diagnosis. Exome sequencing identified the correct gene mutation in 7 of 9 cases; six of these disorders were never before described in the medical literature. Building on these discoveries, **Dr. Robert Jinks and his undergraduate students at Franklin & Marshall** began molecular and cellular research to explore how each specific gene mutation causes neurological disease. Since the pilot study, Broad Institute has identified at least five more genetic conditions in the population. Our preliminary experience with this technology is summarized in a paper submitted to the international journal *Public Library of Science Genetics*.

With generous contributions from Franklin & Marshall College (\$55,000) and Lancaster General Hospital (\$45,000), the Clinic recently acquired an Ion Torrent Personal Genome Machine that will allow us to do this work on site and keep the cost low. As we generate more genetic information, it will be important to organize and store it in a way that is clinically useful.

Through the HHMI Summer Research Fellowship Program at F&M, we are hosting a local high school teacher, Theresa Swenson. She has a Ph.D. in chemistry and her six-week project will focus on the development of an UFFLC method to quantitate ganglioside levels from blood samples. This will be an important tool to determine the efficacy of treatment.

COMMUNITY EDUCATION

Dr. Morton has been busy giving talks at hospitals and universities across the country. He continues his interest in genetic disorders mistaken for child abuse, neglect, and sudden infant death and continues to write and speak about this important topic. Dr. Rider was recently invited to speak to an audience of the world's most respected immunologists at an international conference sponsored by the Jeffrey Modell Foundation in New York City. In April Dr. Strauss gave the Oswald Avery Memorial lecture at his alma mater, Colgate University.

Continuing Education Courses at the Clinic target local pediatricians, family doctors and midwives. We look forward to our upcoming Midwife Education Meeting in August. One of our most important priorities is to educate families. We regularly schedule Family Days to bring leading experts to the Clinic, teach parents what we know about a particular condition, and take the opportunity to hear their questions and learn from them. Within the last few months we've had Family Days for ANT1 deficiency, LMNA cardiomyopathy, Ellis-van Creveld syndrome, SCID, bile salt disorders, and MSUD or Crigler-Najjar families who had or are considering liver transplantation. We look forward to a GA1 Family Day scheduled in July.

Events On the 2011 Calendar:

July 28, Glutaric Aciduria 1 Family Meeting

August 3, Applied Nutrition MSUD Diet Workshop and Dinner

August 11, CME Course for Midwives

August 19-20, EVC Orthopedic Evaluations with Dr. Weiner

CHALLENGING STUDENTS

We are blessed with many bright and dedicated students who have chosen to apply their talents to the study of special children. They bring new ideas and vitality to our work here. In return, they learn something about meaningful work; they learn how to apply their knowledge and focus to people in need.

From Martha King:

After a brief research trip to the Strasburg area in 2008, I spent much of the last year living in Lancaster County doing field research for my PhD in medical anthropology. My work looks at healthcare practices among Amish families in the Lancaster settlement with a special focus on the Clinic for Special Children and the GA-1 families being seen there. The Clinic offers an ideal setting for investigating interactions that occur between patients and practitioners in terms of how we all understand healthcare, genetics, and illness. In addition to providing me with essential research for completing my education, my time at the clinic impacted the way I understand both research and clinic models of care.

Healthcare is approached differently around the country and throughout the world, and CSC's commitment to patient care demonstrates a dedication to their community that is unparalleled in the world of genetic medicine. I have been continuously impressed with the compassion and ardor demonstrated at CSC. During my time there, I also got to witness Drs. Morton, Strauss, Rider, and Puffenberger sharing their experiences and knowledge with other researchers, clinicians working with other Plain communities, undergraduates at Franklin and Marshall College, and visiting medical students. The importance of this kind of outreach can not be understated; informing current practices and future practitioners is paramount in the quest to improve patient outcomes on a local and global levels.

I would like to extend a heartfelt thank-you to everyone who took time out of their busy schedules to talk to me about their family's experiences at CSC. I'd also like to openly thank all of the physicians and clinic staff for their openness and willingness to work with students like myself. We all benefit greatly from their patience and knowledge.

Martha King holds an MA in Folklore and is a PhD candidate in Anthropology at the University of North Carolina at Chapel Hill. She is also a graduate trainee at the Center for Genomics and Society and a dissertation fellow with the National Science Foundation.

From Kiri Sunde, University of North Carolina at Chapel Hill

During my ten-week summer fellowship at the Clinic for Special Children, I am creating a parents' guide to glutaric aciduria type 1 (GA1). As part of this project, I have studied scientific literature on GA1, shadowed members of the Clinic team, and interacted with GA1 patients in the clinic, hospital, and home. The Clinic even arranged for me to live with an Amish family for the summer, and this has formed a very special part of my education. I feel very fortunate to be afforded such a unique and formative experience as an undergraduate student; I cannot imagine another place where I could learn about a problem on so many levels – molecular, clinical, personal, and social – in a single setting.

After spending just one month at the Clinic, I have learned that it's not just the children here who are special. This is a special place full of special people who do special work. Here, the same doctor who exam-

ines your child's sore throat in the clinic also answers your phone calls when you are concerned at home and meets you at the hospital on Saturday night if your child becomes seriously ill. Here, the metric of success is not productivity, revenue, number of publications, or even statistics on patient outcome. Instead, success is measured *one child at a time*: a child with GA1 taking a bite of his second birthday cake; a family without health insurance who can still put food on their table after their infant son undergoes emergency neurosurgery; a family from Brazil who can find a medical home for their special child.

My time at the Clinic has brought me to the frontline of medical science and confirmed my passion for pediatric genetics, but it has also done something greater – it has shown me that medicine doesn't have to be the impersonal, bureaucratic system that prevails throughout the United States. The Clinic is effective precisely because it's not a system – it's a medical home for children who need and deserve personal, comprehensive care. Drs. Holmes Morton, Kevin Strauss, and Nicholas Rider are considered by some physician-scientists at the forefront of genetic medicine, but they view themselves first and foremost as country doctors. They have proven that genomic science can be incorporated seamlessly into primary care. The result of this combination is a special kind of medicine – one that heals, and serves as a standard by which I will judge the many experiences that await me on my journey to become a physician.

From Emilie Muelly, Graduate Student at Penn State Hershey Medical Center:

All parents fear the metabolic crises of MSUD, particularly the risks associated with brain swelling. However, other serious problems such as inattention, depression and anxiety chronically burden many MSUD patients. The underlying mechanisms of these symptoms are not well understood. In collaboration with the Clinic for Special Children, our research team at Penn State is conducting a study to better understand how MSUD chronically alters the structure and chemistry of the brain, how such changes relate to mental illness, and whether or not they can be modified by liver transplantation.

Using Magnetic Resonance Imaging (MRI), we can capture different types of information about the brain, such as the size and structure of different regions, connectivity pathways between different brain areas, and the concentration of specific chemicals involved in nerve signaling and energy metabolism. We are comparing imaging results of MSUD patients to their siblings and correlating these results with blood amino acid levels, medical history, and chronic symptoms. This will allow us to better understand how the chemical disturbances in MSUD chronically damage the brain.

We have begun to analyze data and in general, we found that poor metabolic control is associated with altered brain chemistry, and that these are also associated with the presence and severity of chronic symptoms. So far, our data from transplanted subjects suggest that not all chronic symptoms are reversible in all MSUD patients. Many factors such as the age at which the transplantation occurred and time since the transplantation took place may also influence outcomes.

In the past two years, I have learned a great deal from this collaborative project. I particularly thank the physicians at the Clinic – their genuine care and love for their patients and their mastery of the science underlying these rare disorders allows them to be the ultimate role models for me as I train to be a physician who does research. I also want to thank those who have volunteered for the study! Getting to know you and your families has been a tremendous blessing.

Kristin Boulter, Johns Hopkins University:

Last summer a magazine article planted the first seeds of my desire to spend time at the Clinic for Special Children. For me, a pre-medical molecular biology major at Johns Hopkins with a long-standing inter-

est in genetics, a place that linked preventative treatment with research seemed too good to be true. The control of confounding variables normally plaguing such investigations and the gorgeous terrain provided by the unique setting of Lancaster County clinched the deal for me. A few emails and months in Dr. Kelley's Baltimore lab later, I was thrilled to be starting work on propionic acidemia, one of the 108 genetic disorders seen and treated in the well built clinic.

My work here has been compiling and analyzing metabolic data collected over the past few years from patients both in sickness and health, treated and untreated and with various complications. Hopefully, the data will provide a way to discern what kind of treatment, if any, disease variants can benefit from and identify children at risk for more dangerous complications such as cardiomyopathy and its associated heart failure. While the more academic work has been rewarding, what makes my experience almost magical is the daily interactions with doctors and patients. Even in the short weeks I have been here, I feel I have learned so much not only about the disorders but the preventative strategies and dedication of doctors and families that have made this clinic so successful in fulfilling its mission.



From Lauren DuBiner, F&M College:

During the Spring semester of my junior year, I took the course offered at Franklin and Marshall College called Plain People, Modern Medicine taught by Drs. Morton, Strauss, and Puffenberger from the Clinic for Special Children. I immediately realized what an important job these individuals had and knew that I wanted to be a part of it. I chose to pursue an independent study with Dr. Strauss that would be a continuation of the information I learned from the course about translational medicine. My independent study focused on the development of natural history and documentation of disease progression of ANT1 deficiency in the Mennonite population. The patients with ANT1 deficiency displayed hypertrophic cardiomyopathy, severe fatigue, and lactic acidosis. While I immensely enjoyed learning to analyze echocardiograms and discovering unexpected trends in the data, the most rewarding part of this experience was meeting the patients. During the screening day on March 1, I had the honor of getting to know all of the patients with ANT1 deficiency and their families. Being able to put faces with the names I had seen on my Excel spreadsheet was indescribable. My analysis of the March 1 data revealed many novel findings that I hope will aid in developing a more effective clinical course.

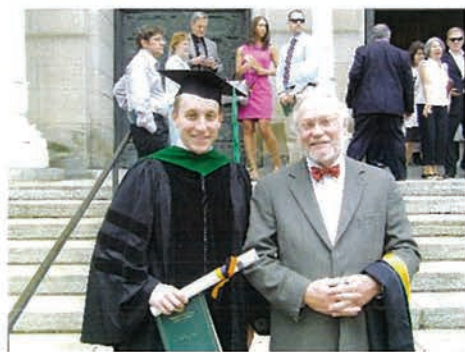
Theresa Swenson, Ph.D., a high school chemistry teacher at Elizabethtown Area High School, is participating in a six week summer research fellowship in bioinformatics at the Clinic. Franklin and Marshall College, through a Howard Hughes Medical Institute grant, partnered with the Clinic to offer this opportunity to high school teacher applicants. Theresa has a B.S. in both Biology and Chemistry, a Ph.D. in Physiological Chemistry (from the University of Wisconsin) and did a post-doctoral fellowship at Columbia University in New York City. Her research background is in lipid biochemistry, and this will be especially helpful with her project at the Clinic.

Last summer I enrolled in a Bioinformatics seminar at Franklin and Marshall College and during that time had the opportunity to meet both Erik Puffenberger and Kevin Strauss, and learn more about the Clinic and its Mission. I was so impressed by their work that I applied for a bioinformatics fellowship to work at the Clinic this summer. By working at the Clinic on a daily basis I will bring my biochemistry knowledge up-to-date and use that knowledge to develop lessons for my students and get them excited to participate in research projects that will hopefully inspire them to further their education in science.

I am working on developing a clinical assay to detect changes in certain gangliosides and other glycolipids that are distinctive in individuals with a mutation in a gene that codes for GM3 synthase. Individuals that lack a functioning GM3 synthase develop a syndrome called Amish Infantile Epilepsy Syndrome. In addition to epilepsy, affected individuals suffer developmental stagnation and blindness. The development of a clinical assay for this disorder will give the physicians at the Clinic a tool to monitor the time course of the disorder and follow the efficacy of medical interventions used to alleviate the symptoms of the disorder.

CONGRATULATIONS !

Michael Fox was a student in the first class taught by Holmes Morton, Kevin Strauss and Erik Puffenberger four years ago at Franklin & Marshall College as the Clinic, F&M, and LGH began their partnership in education and research. He was the first F&M Eyer Fellow to study at the Clinic during the summer of 2007 following his F&M graduation. His reflections about his experience with the Clinic were in the Summer '07 Newsletter.



In May, Mike graduated from the University of Pittsburgh Medical School, a leader in his class, with Dr. Morton delivering the graduation address and among the first to congratulate him. Mike will continue his education in

pediatrics at Pittsburgh Children's Hospital. All of us at the Clinic congratulate Dr. Fox and look forward to arranging a clinical rotation with him in the future.

Measles Outbreak –

A Reminder of the Importance of Vaccination

---Dr. Rider

We are fortunate individuals living in a country where good medical care and clean drinking water are readily available. One of the most important advances in modern medicine is the provision of purified, effective vaccines to prevent serious illness and death due to once common childhood diseases. Most importantly, vaccines are available to help spare death and disability; however, they also prevent cata-

strophic illness resulting in lengthy hospital stays and hundreds of thousands of dollars in healthcare bills.

A reminder of the potency of these diseases became evident in Europe recently. Over the past two years 6500 cases of Measles were reported by 33 countries throughout Europe. In France alone, 4937 Measles cases occurred between January and March 2011. Similarly, in 1991 Pennsylvania was one of five states reporting a Rubella (German Measles) outbreak. During this outbreak almost 900 of the 1093 individuals who became sick were from the local Amish community. Twelve Amish babies were born with congenital rubella syndrome, which can cause deafness, cataracts, congenital heart disease, permanent neurological disability or death of an unborn baby.

Both the European Measles outbreak and the 1991 Pennsylvania Rubella outbreak resulted from large numbers of unvaccinated people becoming ill and spreading the disease to other unvaccinated individuals. We recommend that all infants and children be evaluated for routine vaccination. Most individuals should receive all recommended childhood vaccines. Vaccines are available at the Clinic for Special Children or through the local state health department.

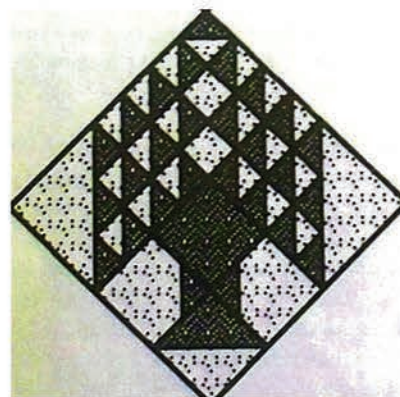
A FAREWELL

It is with great regret that we announce Dr. Nicholas Rider will leave the CSC staff as of September 1. Dr. Rider has been a highly valued and respected member of our staff for the past three years and we will miss him. He shares his farewell in the following letter:

Dear Colleagues and Friends,

It has been my pleasure to work at the Clinic full-time for 3 years following 2 years of student research. Through this period, I have enjoyed tremendously gratifying work with truly outstanding people. My work at the Clinic has been both humbling and inspiring; I will always be thankful for the experience. This spring, I decided to make a change for personal reasons and will leave full-time work at the Clinic in September 2011. My hope is to remain involved in a different but still meaningful way moving forward. I will continue to cherish the experiences I've had and look forward to future opportunities to see the many important people (friends, colleagues, patients and families) who mean a great deal to me. This decision was difficult for me personally and cannot be easily summed up; however, I will leave with a quote that touches upon the process and focus of my decision - "He is no fool who parts with that which he cannot keep to gain that which he cannot lose." ~the late Philip James Elliot (October 1949). Thank You!

*Sincerely,
Nicholas L. Rider, D.O.*



~ Searching for a Special Pediatrician ~

The Clinic is beginning its search for a physician to join the staff as a pediatrician with a strong interest in genetics.

“... caring for the patient,” seeing the patient whole, broad medical knowledge and a passion for applying it in a clinical setting, respect for people from diverse cultures, determination, tenacity, energy, strength, stamina, courage to examine difficult conditions and decide what to do , an extraordinary, unquenchable desire to know - are all characteristics, which will define a successful candidate.

New CSC Board Members

The Clinic welcomed two new members to the Board of Directors in recent months. Mark Martin and Herman Bontrager, joined the Board in December. We are grateful for their time, wise counsel and willingness to serve.

PROPIONIC ACIDEMIA: NEW CONCERNS ABOUT A COMMON DISORDER

Holmes Morton, MD

with Kristin Boulter and Nikolas Muenke

Kristin Boulter is a pre-medical student from Johns Hopkins who has worked in Dr. Kelley's lab at Kennedy Krieger. Kristin has been sorting a complicated collection of clinical, cardiac, and laboratory data about patients with PA. Nikolas Muenke set-up quantitative measurement of normal citric acid cycle metabolites and the pathological chemistries associated with PA.

We were forced to rethink our approach to therapy when a 17-year-old patient who was on therapy presented during a common respiratory tract illness with severe heart failure. About the same time heart studies of another patient showed poor heart function despite current therapy. More recently a 3 year old Amish patient, whose undiagnosed brother died of heart failure, presented in coma with severe metabolic illness.

In each of these cases the patients were treated with more limited dietary protein, a mixture of amino acids similar to those used in our metabolic formulas for MSUD and GA1, and medications for heart failure. In two patients heart failure did gradually reverse. Remarkably, the 3-year-old Amish boy emerged from metabolic crisis and coma without brain damage or heart failure.

We currently care for 34 patients with Propionic Acidemia from Pennsylvania, Maryland, New York, Ohio, and Indiana. We are aware of Amish and Mennonite PA cases in Missouri, Iowa, Wisconsin, and would expect to find cases in most Plain populations of North America. The majority of PA patients over age 10 are unrecognized because Newborn Screening has detected cases of PA in the United States and Canada only in recent years. An Amish family from Ohio recently reminded us of the vulnerability of these unrecognized patients. The family learned that 4 of its grown children had PA and severe heart

problems. One teenage boy died of a sudden cardiac death, probably the result of an arrhythmia in his failing heart. Another 24-year-old man had to undergo heart transplant because of end-stage heart failure. A 30 year-old mother of 4 was found to have poor heart function and irregular heart-beats and needed a pacemaker.

In addition to the Clinic's patients, Akron Children's currently cares for 25 children with PA. Dr. Olivia Wenger, now on staff at Akron Children's, organized a meeting with cardiologists, geneticists, and hospital administrators about the need for changes in the approach to caring for patients with PA.

MEDICAL PROBLEMS:

The Amish and Mennonite variant of PA was believed to be a relatively mild form of the disease because a majority of untreated patients remain asymptomatic in infancy and early childhood. In contrast, a newborn with a severe form of the disorder can deteriorate and die of overwhelming metabolic illness in the first few days of life. Metabolic crises with lactic acidemia, keto-acidemia, high ammonias, and low blood sugar are associated with recurrent vomiting, seizures, and coma. Basal ganglial strokes, similar to those seen in patients with glutaric aciduria (GA1) do occur. As was true for GA1 before 1988, undiagnosed children and adults with PA who have had this form of brain injury were often said to have "cerebral palsy."

Since 1995 the 34 patients seen at the Clinic have had 30 hospitalizations, only 9 of these were at Lancaster General Hospital. As is true for MSUD and GA1 the majority of these hospitalizations for metabolic illnesses were provoked by a common infections like rotavirus, RSV, or influenza. When metabolic intoxication of the brain develops, patients often have seizures or strokes and become unresponsive. Recovery may be incomplete, leaving children and adults neurologically disabled.

Life-threatening heart failure and irregular heartbeats are problems for this group of patients. We are aware of 1 sudden cardiac death, 3 deaths from heart failure, 1 heart transplant, and 2 patients living with moderate and severe heart failure. At least 9/34 (23%) patients are known to have significant heart problems. Published reports estimate that 25% of all PA patients worldwide have heart problems by 8 years of age.

Heart failure, sudden loss of conscious ("fainting") or sudden death from heart arrhythmias will probably be the most common presentation of undiagnosed cases of PA in older children and adults from the Amish and Mennonite Communities. At the time of diagnosis a patient should routinely have a cardiac echo, EKG and a 24-hour Holter-monitor as baseline studies. These studies should be repeated at least once yearly, and at anytime the patient experiences illness or complaints of fainting, irregular heartbeats, fatigue or shortness of breath during normal daily activities.

WHO SHOULD BE TESTED?

The first step in treatment is diagnosis of the condition in the healthy newborn or child. **ALL NEWBORNS SHOULD BE TESTED.** We prefer sending Supplemental Newborn Screening samples on all infants to the Perkin-Elmer Lab in Pittsburgh Pennsylvania:

Perkin Elmer Genetics

90 Emerson Lane , Bridgeville, PA 15017

Tel: 412.220.2300 or 866-463-6436; Fax: 412-220-0784

WEB: <www.perkinelmergenetics.com>

The Clinic For Special Children offers targeted mutation testing for PA, which detects patients who have inherited two abnormal copies of the PCCB gene, as well as carriers, who have one normal and one abnormal copy of PCCB. All Amish and Mennonite propionic aciduria

patients have the same mutation in a gene-protein PCCB (1606A>G). We believe this is one of the more common biochemical disorders in the Plain Populations of North America. The Clinic's lab also offers biochemical studies of urine organic acids and plasma amino acids, which are used to monitor treatment of the disorder. Whole blood or plasma propionyl-carnitine levels are measured through the Perkin-Elmer Genetics or Mayo Clinic Laboratories.

We also recommend testing all siblings and parents of newly diagnosed infants and children, regardless of their prior health history. Screening for Propionic Acidemia in Ohio, New York, and Maryland only started in the early 2000, about 10 years after Pennsylvania. Older children and adults with unexplained episodes of ketosis, seizures, loss of consciousness, or those with heart failure, arrhythmias, or a disability called "cerebral palsy" should also be tested. High risk infants should be tested using cord blood on the day of birth.

TREATMENT OF PROPIONIC ACIDEMIA:

The goal of treatment is to prevent metabolic illnesses, seizures, strokes, mental retardation, sudden death, heart failure, and limit hospitalizations. Dietary protein restriction with biotin, carnitine, and pantothenate supplements probably do decrease the risk of severe illness and heart problems, but this therapy does not completely control the disorder. Even patients who carefully follow a prescribed diet remain at risk for seizures, strokes, and heart problems, especially during infectious illnesses when fasting or even with prolonged exercise or heavy work.

Patients managed in this way appeared to be healthy and had few hospitalizations. Our cases of severe illnesses and heart problems were usually found in patients who were undiagnosed and untreated, similar to those in the Amish family from Ohio.

NEW IDEAS ABOUT THE TREATMENT:

Since February 2009 we have increased the number of blood chemistries, amino acids, organic acids, EKGs and heart studies done during routine visits and illnesses for PA patients. Most of these studies have been paid for through the Clinic's Research and Education Fund account. \$15,275 has been written off patient accounts to help underwrite our studies.

The toxicity of PA is, we now believe, directly related to the accumulation of propionyl-CoA in the mitochondria of the heart and brain. Toxicity to the kidney, liver, skeletal muscle, and other tissues is limited but may become important during extreme illnesses or even with sustained exercise. Toxicity to heart and brain can be prevented, or to some degree reversed, by limiting the dietary intake of amino acids and odd chain fatty acids that form propionate. Antibiotics also suppress intestinal bacteria that produce about 20% of the daily propionate load, but, the therapeutic value of this is unclear.

The biochemical goals of this therapy are to prevent or reverse ketosis and maintain a high citrate/methylcitrate ratio and high sum of citric acid cycle intermediates. It is especially important to maintain intake of high sugar drinks and these supplements during illnesses. Citric acid itself can be given as polycitra – a sweet fruit flavored liquid taken with juice or Tang. If a patient with PA stops taking the citrate and amino acid mixture, stops drinking and eating, starts vomiting and has moderate- to- large ketones in the urine, then hospitalization is needed.

AMINO ACID TRANSPORT AND THE TREATMENT OF PROPIONIC ACIDEMIA:

We are working with Applied Nutrition to help manufacture a formula for the management of PA that provides an amino acid mixture that will serve both the anaplerotic function and help limit heart and brain uptake of isoleucine, valine, and threonine. The formula will also have the calories and nutritional make- up of an infant formula and the standard minerals and vitamins required for metabolic formulas. The effects of this new formula will be monitored by frequent blood counts, chemistries, amino acid profiles. Similar studies were used to develop more effective treatments for MSUD and GAI.



The Science and Economics of Prevention

Kevin A. Strauss, M.D.

The Human Genome Project has generated a landmark catalog of information about genes and their role in disease. However, researchers agree that we could do a better job of using this knowledge to help people. Much time and money are spent on large, expensive genetic studies that do not really benefit patients. Meanwhile there are many people, especially children, who continue to suffer from genetic diseases. This is tragic, because we have learned that integrating the special knowledge of biochemical genetics into everyday medical practice can prevent many terrible outcomes. Some critics worry this approach is not sustainable but our experience over 20 years suggests otherwise.

The Clinic economy is trivial compared to U.S. health care spending but differs qualitatively in important respects (Table 1). In 2010, the Clinic spent 1.5 million dollars providing laboratory services and comprehensive outpatient care for 1877 patients (\$799 per patient) and offered testing for 103 different gene mutations. Ninety-five percent of our patients are uninsured and the Clinic receives no state or federal money. The budget grows 3.6% per year. One third is raised at annual quilt auctions, one third represents charitable gifts from individuals, and the additional third is fees. By comparison, 2010 medical spending for the U.S. population was \$8,344 per person, half of which was paid by state and federal governments. This spending increases 6 - 7%

per year. The National Institutes of Health spent 31 billion dollars on biomedical research in 2010. Eight billion was categorized as research involving genetics; only 3% of this was allotted to research on gene therapy or direct patient care.

Table 1. Medical Spending: United States versus Clinic for Special Children

	U.S.	CSC
Patient population	311,000,000	1877
Annual cost	2.5 trillion	1.5 million
Per capita cost (U.S. dollars)	\$8,160	\$779
Per capita government subsidy	50%	0%
NIH-funded medical research	31 billion	0
Annual medical inflation rate	6.1%	3.6%
"Return" on investment of \$1	?	\$15

Within this broad context, how can we measure the value of the Clinic for Special Children over its 20-year history? Parents who struggle to care for a special child might say that the support and hope they find at the Clinic is invaluable and needs no justification in financial terms. It is nevertheless instructive to examine the Clinic's impact in concrete economic terms. To do this, we can define value as "health outcomes per dollar spent" and focus on outcomes that matter most to patients: survival, well-being, independence, and freedom from pain. We consider cost from the patient's perspective, extrapolating dollar amounts from real hospital bills, and use outcome measures for which medical spending can be confidently measured: diagnostic efficiency, hospitalization, and disability prevention.

MEASURING VALUE LOCALLY

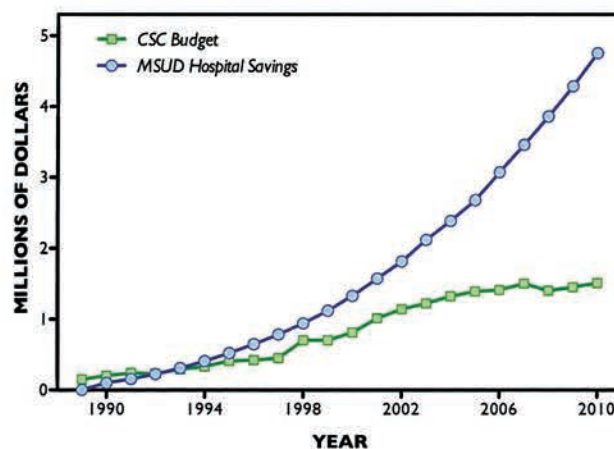
More Efficient Diagnosis

When parents of a disabled or ill child seek testing to determine the cause, evaluation at a large university medical center typically includes a battery of expensive tests. These diagnostic excursions are often protracted and wasteful; our review of contemporary hospital billing records indicate that each costs between 20 and 40 thousand dollars for a diagnostic yield of 25-50%. Each year, the Clinic invests the equivalent of just one such workup, about 35 thousand dollars, on research used to map and develop testing for genetic causes of childhood disease. As a result, more than 100 genetic disorders can now be diagnosed in our office within 2 days for \$50-100. In aggregate, such testing saves local Plain communities about 700 thousand dollars per year. Additional on-site testing (e.g. amino acid analysis, genetic carrier testing) saves families about 900 thousand dollars annually and reduces wait time by more than 16,000 patient days per year (Table 2).

Lower Hospitalization Rates

Diagnosis is just the start; to prevent catastrophic outcomes and runaway costs requires a high level of clinical commitment. Consider just one disorder: classical MSUD. Before 1989, Mennonites born with MSUD arrived critically ill to regional pediatric centers where they stayed an average of 12 weeks. These hospitalizations cost 50 thousand dollars or more; one third of patients died and most who survived were severely disabled. Beyond infancy each patient was hospitalized about once yearly for an average of 7 days, which today would cost an average of \$8,000 per day (range \$1,000 to \$38,000 per day). Nowadays, about half of the Mennonite babies born with MSUD are diagnosed using inexpensive on-site genetic testing that is complete within 24 hours of life, before the child becomes ill. Progressive improvements in outpatient monitoring and treatment have decreased hospi-

talizations from 7.0 to 0.1 days per patient per year. This 98.5% decrease in hospital costs applied to 81 MSUD patients under our care saves the community at least 4.3 million dollars annually--nearly three times the Clinic's operating budget (Fig. 1).



Disability Prevention

Half the disorders we manage at the Clinic cause neurological disability and many of these are treatable. In 2004, the Centers for Disease Control and Prevention estimated costs associated with four major types of disability: mental retardation, cerebral palsy, hearing loss, and visual impairment. Estimated lifetime costs are attributable to medical care, assistive devices, transportation, special education, and lost productivity of disabled individuals and their caregivers. The CDC estimates these lifetime costs to be between \$630,000 (hearing loss) and \$1,530,000 (mental retardation) per affected individual. Since 1989, we have been able to prevent major disability (e.g. generalized dystonia, spastic paralysis, stroke, cognitive impairment, blindness) in at least 200 children (10% of patients under our care). This has saved the Plain communities about 270 million dollars. The Clinic's cumulative operating cost over this same period was 18.3 million dollars.

Reduced Hospital Bills

The United States has the most expensive health care in the world. Increasingly, we feel the cost of medical care for special children threatens their quality of care. Some families refuse costly surgery or urgent hospitalization because they fear it could impoverish them; others bring their children to the hospital reluctantly only to worry daily about how long they must stay. We take these financial concerns seriously, but they cannot be weighed against the value of human life. To relieve this stress, we've worked with all four major pediatric referral centers - Lancaster General, Children's Hospital of Philadelphia (CHOP), Hershey Medical Center and, most recently, Nemours A.I. duPont Hospital for Children—to establish fair billing policies for uninsured families.

Through these negotiations, all four medical centers now provide at least 70% discounts to our self-pay patients. Recent follow up data from CHOP shows the financial impact of this policy. For the 23 children we referred to CHOP over the last 12 months, the 70% discount has saved Plain communities more than \$900,000. Applied to all four referral hospitals, economic arrangements forged by the Clinic will constitute about 2 million dollars in annual savings. A minority of families don't meet eligibility for discounts at LGH. We collaborated with LGH to create the Children's Hospital Fund, to pay 50% of hospital bills for families ineligible for LGH financial assistance. Since its inception in early 2010, the Children's Hospital Fund has paid out \$86,500 to help families in need.

SCIENCE, ECONOMICS, AND THE CARE OF SPECIAL CHILDREN

Much of the Clinic’s success rests on the products of modern science. However, what makes the Clinic different is how we define the proper distribution and use of that science. As stated plainly by one researcher a decade ago: “stunning scientific and technological advances in genetics will mean little if they do not benefit people” (Guttmacher et al., 2001). An abiding principle of the Clinic is to keep scientific research firmly rooted in people’s everyday needs; these needs drive innovation and shape how we use technology. Because our lab was deliberately designed to serve a particular community, we can provide families with meaningful clinical information at 10-40% the prevailing cost and in a fraction of the time (Table 2). Thus as our clinical responsibilities grow, the scientific mission remains focused on access, affordability, and prevention. In practical terms, this means that dangerous conditions can be diagnosed on site for less than \$100 within a few hours or days of life and treated locally to prevent hospitalization, disability, and death.

This approach has a measurable effect on community health: 41% of the disorders we manage can be treated decisively and for an additional 36%, informed medical care allows children to suffer less and live more independently. Figure 2 shows projected savings from reducing testing, hospitalization, and disability among Plain populations over the next 10 years. These calculations assume the population grows 5.5% per year and medical inflation continues at its current rate.

Present investment in the Clinic pays off 15 to 1: operational spending of 1.5 million dollars saves the community about 24 million dollars per year (\$12,800 per patient per year).

These figures will seem astonishing to many readers. Indeed, money saved cannot be counted with certainty, but remember that our estimates are based on the real hospitalization rates, hospital bills, and disease rates experienced by our patients. Overall cost savings depend on investing more in some services (e.g. molecular diagnostics and preventative treatment) to reduce the need for others (chronic care). This type of analysis is a reminder to critics who would question the wisdom of operating sophisticated technologies in under served or rural settings.

The estimates of cost savings for families and the communities the Clinic serves are significant. However, each year the Clinic struggles to meet its modest operating budget. Despite generous gifts from our many supporters and the reliable income from auctions, it is a challenge to meet our annual operating costs. We need more help to sustain our work year to year to continue to improve care for children. We need your help.

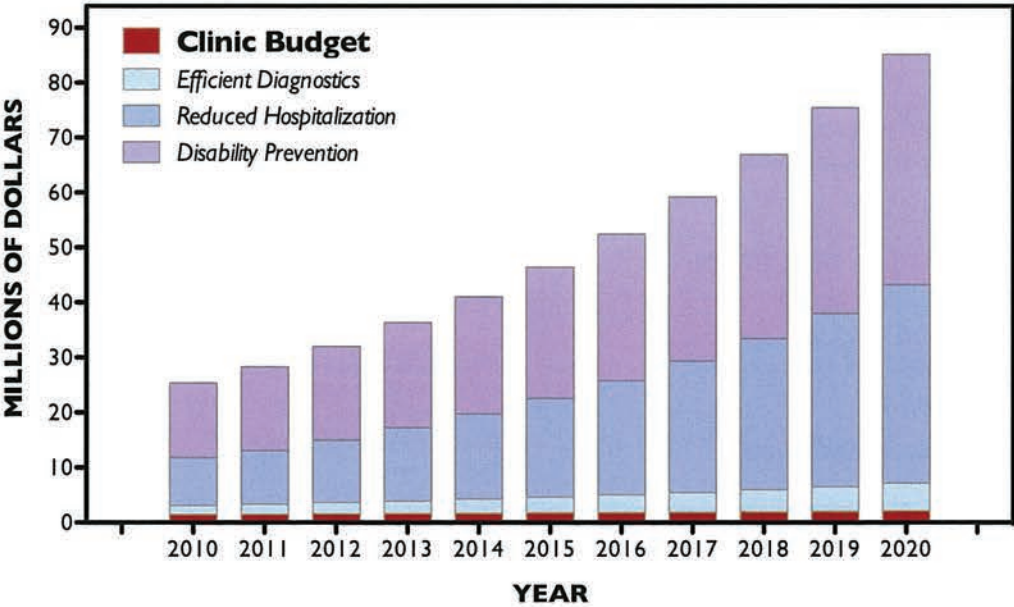
Please consider a major gift to the Clinic for Special Children. In the world of biomedical research and quality health care, our goal is modest. Over the next 5 years, we hope to raise 10 million dollars for the Clinic’s Research, Education and Sustainability Fund. This will generate the annual income we need to guarantee affordable health care, a medical home, for special children of the next generation: your grandchildren and great grandchildren.

Table 2. Comparison of Price and Turnaround Time for Laboratory Services

	Commercial Lab*		University Lab†		Clinic for Special Children Lab				
	Cost (U.S. dollars)	Turnaround	Cost (U.S. dollars)	Turnaround	Cost (U.S. dollars)	Turnaround	Number per year	Dollars Saved	Time Saved (Days)
Amino acid analysis	700	5 days	240	4 days	75	45 minutes	1310	\$517,450	5856
Organic acid analysis	247	6 days	230	6 days	85	4 hours	175	\$26,863	1024
Targeted detection of known gene mutations§	590	14 days	225	21 days	50	1-2 days	405	\$144,788	6480
Complete gene sequencing, cost per exon	147	11 days	148	28 days	35	5 days	15	\$1,688	218
Cytogenetic microarray (DNA copy number)	1,654	21 days	1,550	28 days	600	4 days	145¥	\$222,290	2973
Totals								\$913,078	16,549

*<http://www.mayomedicallaboratories.com/test-catalog/>

†<http://www.bcm.edu/geneticlabs/>



Clinic for Special Children
P.O. Box 128
Strasburg, Pennsylvania 17579



2011 BENEFIT AUCTIONS:
July 9, Shiloh, Ohio
July 16, Shippensburg, PA
September 10, Blair County, PA
September 17, Lancaster County, PA

MISSION

The Clinic for Special Children was established in 1989 is a non-profit medical service for Amish and Mennonite children with genetic disorders. The Clinic serves children by translating advances in genetics into timely diagnoses, and accessible, comprehensive medical care, and by developing better understanding of heritable diseases.

CLINIC FOR SPECIAL CHILDREN

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