



CLINIC FOR SPECIAL CHILDREN NEWSLETTER

VOLUME I NUMBER 32

* LANCASTER COUNTY, PENNSYLVANIA *

WINTER 2011

~ GREETINGS ~

WITH OUR WISH THAT ALL WILL SHARE THE SPIRIT OF JOY,
REJOICE IN THE GIFT OF HOPE
AND GROW IN UNDERSTANDING THROUGH CARING FOR OTHERS

We are very grateful for the support received from this year's benefit auctions. All four events were well attended and bidding was generous. Support from the auctions provided 1/3 of the annual funds needed to operate the clinic. The **Shiloh, Ohio** auction held in July featured 22 quilts and many pieces of handcrafted furniture for a record crowd. In **Shippensburg, PA**, 29 quilts, a new wagon, furniture and many garden items kept bidders busy. Contacts for the Shippensburg auction are Elvin Oberholtzer, chairman, 717 532-9088; David Zimmerman, treasurer, 717-532-5221 and David Leinbach, committee member, 717-532-3642. The auction at Morrison's Cove in **Blair County** also featured 29 beautiful quilts. Locally made furniture, great chicken barbecue, soft pretzels and plants for fall attracted many bidders from the central region of Pennsylvania.

The Leola Produce Auction was the setting for the 21st year of the auction in **Lancaster County**. The same group of dedicated volunteers who planned the very first auction for the clinic in 1991 are still on the auction committee. We are very thankful for their faithful and enthusiastic support. The auction featured 89 quilts this year, several locally made furniture sets, sheds, swing sets, toys, gift certificates and several unique items such as two complete, bound collections of every issue of our Newsletter. And, food.....



2011:
3200 Subs
18,000 Donuts
500 Smoothies
4000 Soft Pretzels
530 gallons of Ice Cream
Ham & Cheese Sandwiches
2637 pounds of Barbecued Chicken
3700 pounds of Potatoes for French Fries & Chips
Fried Pies, Fruit Pies, Whoopie Pies, Pizza Pies
Salad Bar, Fruit Cups
600 Pancakes
700 Omelets
Baked Goods
8 Roasted Pigs

Thank you to all who volunteered; to all who donated sale items and food; to all who came; to all who bid; to all who enjoyed 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.

LOOKING AHEAD.....

BENEFIT AUCTION DATES FOR 2012

July 14, Shiloh, Ohio
July 21, Shippensburg, PA
September 8, Blair County, PA
September 15, Lancaster County, PA

A MATCH OF SUPPORT !!!

We thank a Lancaster area family foundation for their matching challenge gift of \$50,000. With generous contributions from 57 donors, we met the challenge by mid October. We continued with our goal of doubling the challenge and as of mid December, we met the challenge a second time.

Many have given so generously!! We are very blessed to have support from the communities we serve and from faithful donors from all across the U.S. Thank you to all for this much needed support.

ANOTHER KIND OF MATCH

September is always a busy time at the Clinic with two auctions and many families coming for clinic visits from other regions of the country. This year we were especially busy as we worked with a family whose baby was born the week of the auction and diagnosed by the Clinic with severe combined immune deficiency (SCID IL-7 Receptor). The family knew they were at risk for IL -7 after their son, born in 2003, died of complications from the disease at the age of six months. He had received a bone marrow transplant at Children's Hospital of Philadelphia (CHOP) at the age of 5 months after diagnosis. One thing the family knew is the faster the diagnosis can be determined, the better the chances for a healthier baby. Once alerted of the birth, the Clinic halted all renovation work in progress in the lab so equipment could be used without interference. Diagnostic tests confirmed IL -7 and the Clinic immediately began the process to perform HLA typing of family

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 Eyerl 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 Pittsburgh as a resi-

dent 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.

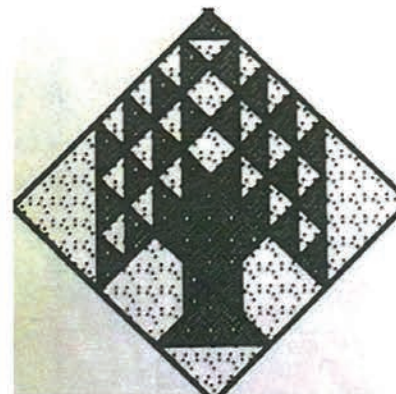
A FAREWELL

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

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

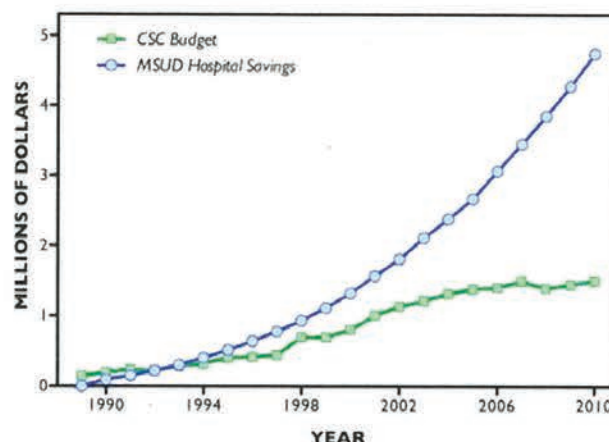
More Efficient Diagnosis

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.

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 GA1.



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%

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.

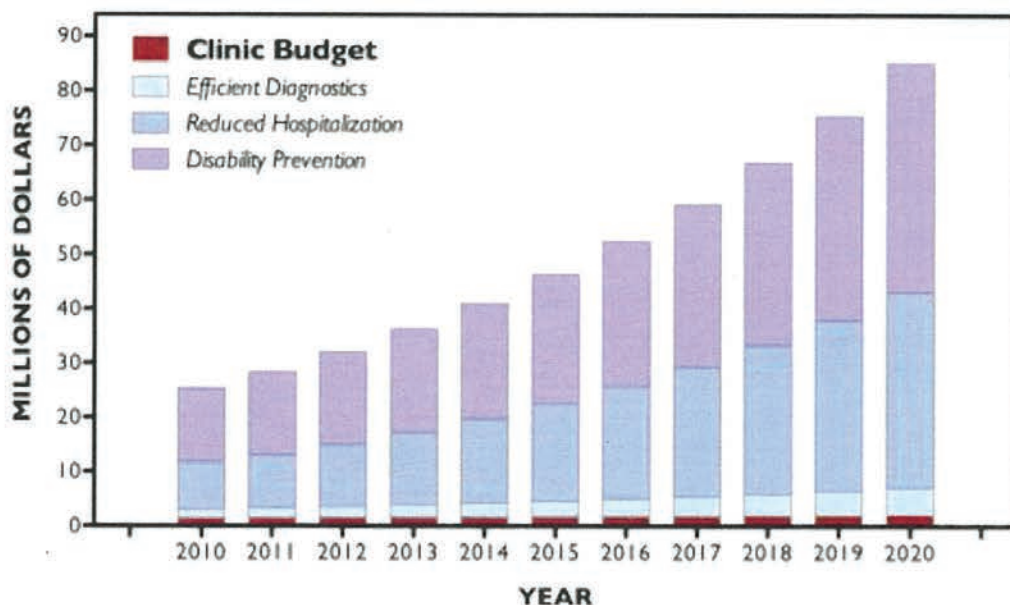
Please consider a major gift to the Clinic for Special Children. In the world of biomedical research and quality health care, our goal is modest. Over the next 5 years, we hope to raise 10 million dollars for the Clinic's Research, Education and Sustainability Fund. This will generate the annual income 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	4 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	1454	\$222,290	2973
Total								\$913,078	16,549

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

†<http://www.bcm.edu/geneticslab/>



In **Shippensburg, PA** bidding on a new locally made carriage brought a good price while Dr. Morton and Dr. Strauss tried it out. The auctioneer made it clear the two doctors from the Clinic for Special Children were not included in the sale price. Hand made toys, quilts, furniture, landscaping plants and a wide choice of food were available for buyers. Thousands of donuts made that morning at the sale sold out by early afternoon. Next year the Shippensburg Benefit Auction will be held on June 22, 2013, the 4th Saturday of June instead of the third Saturday of July. Thank you to the Oberholtzers, Zimmermans, Leinbachs, and many other families in the Shippensburg region for this wonderful support.

TWO TO GO

Coming up in September are two more auctions. The first is in **Blair County, PA on September 8th** at Morrison's Cove Produce Auction on Route #36 south of Roaring Spring. In addition to quilts, furniture and similar items offered at all of the other auctions, this sale always has a beautiful array of mums to get us ready for fall. For our supporters in Pittsburgh, it is not so far to go to bid on a beautiful quilt! We hope for a big turn out in Blair County.

The last and final auction of the year is in **Lancaster County on September 15th** at the Leola Produce Auction, Brethren Church Road, Leola, PA. Once again and for the 18th year one of the special quilts made for this auction is the Postage Stamp quilt. Pieced with



one by one inch squares and hand quilted and dated by an aunt of a very special Clinic patient, the Postage Stamp quilt is always a favorite among bidders. Over the past seventeen years, this quilt design has brought over \$25,000 in support for the Clinic. We are grateful for every patch and stitch!

The Postage Stamp quilt for 2012 in progress.

A PREVIEW.....

Another item made for this year's auction will be a unique ice cream machine expertly handcrafted by the father of a special child who is a patient at the Clinic. It features a new working model, 1/2 scale, 1/2 horsepower New Holland Hit and Miss engine with a one quart Limited Edition Country Ice Cream Freezer mounted on a wooden wagon platform engraved with the *Clinic for Special Children*. It is beautifully made and one of a kind. And, it actually makes a quart of ice cream! Choose your own flavor!



Other items to be auctioned include a new Amish carriage with LED head and tail lights, scrolled oak switch box, easy light springs, wooden wheels and a navy blue interior and a new aluminum spring wagon. Sheds, swing sets, garden

items and furniture in addition to numerous handmade quilts in many popular colors and patterns will be available. We hear there will be one, perhaps two expertly crafted state of the art Martin Bird Houses donated for the sale.

Bidding will start at 8:30am and continue until everything is sold. Dr. Morton and Dr. Strauss will give their annual remarks at 11:00 a.m. Quilts, special items and furniture will be sold after their remarks.



A MATCH FOR SUPPORT !!!

We have a matching gift challenge for 2012. A Lancaster area family foundation is giving us a challenge to match \$25,000 by December 1, 2012. Please help us not only to meet this challenge, but to double match it by December 1st! We need the support and your help to reach our goal.

UPDATES: PROGRESS IN 2012 RESEARCH AND CLINICAL CARE

GM3 Synthase Deficiency - A family meeting held on **May 11th** at the Peachey's in Lewisburg, PA, was well attended by families from Pennsylvania and Ohio. CSC and DDC clinic in Middlefield, OH, are partnering in a clinical trial of oral replacement therapy of Ganglioside-500 a product developed and donated by Fonterra. F&M students continue their work on an injectible form of GM3.

Pretzel Syndrome, July 19th - Families of children with "Pretzel Syndrome" gathered for a picnic and fellowship on the Zimmerman's farm in Ephrata, PA. The Clinic is in collaboration with a team directed by Dr. Peter B. Crino, Director of the PENN Epilepsy Center at the University of Pennsylvania with the goal of understanding the syndrome and developing an effective treatment.

August 17 & 18, Dr. Weiner, pediatric orthopedic specialist from Akron Children's Hospital will evaluate patients at CSC.

September 5th, Otosclerosis Day for Extended Families with Dr. Rob O'Reilly and his team from A. I. DuPont Hospital for Children.

Dr. O'Reilly and his team from A.I. DuPont partner with CSC to provide audiology services at CSC on a monthly basis.

September 14, Treatment of Propionic Acidemia

This conference, sponsored by CSC, will include discussion of a 2 year trial of a new formula designed to protect the heart, brain and prevent metabolic crisis. The formula, Propionade Junior, was developed by Applied Nutrition and CSC.

Midwife CME course - A Review of the Genetic Causes of Stillbirth & Asphyxia. Newborn Resuscitation and the use of Hypothermia in the care of the Asphyxiated Newborn. Date to be determined.

Clinic for Special Children
P.O. Box 128
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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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PA law requires us to advise that a copy of our official registration and financial information may be obtained from the PA Dept. of State by calling toll free 1-800-732-0999. Registration does not imply endorsement.