



**Amish Research Clinic**  
**At the Clinic for Special Children**  
**535 Bunker Hill Road, Strasburg, PA 17579**  
**717-687-8371**



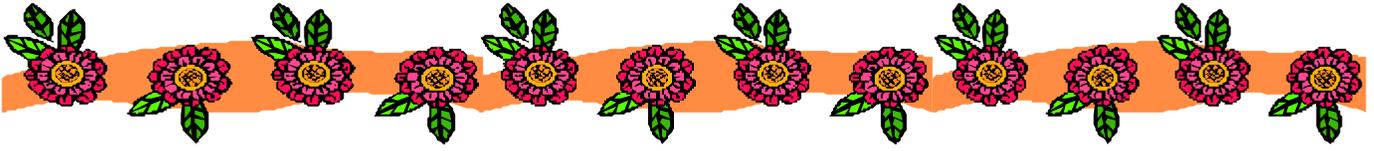
It is hard to believe that we are celebrating our 11<sup>th</sup> year since the opening of the Amish Research Clinic in 1995. During that time, we have seen nearly 4,000 Amish volunteers walk through our Clinic doors to participate in research studies on diabetes, osteoporosis (weak bones), high blood pressure, cholesterol abnormalities, heart disease, breast density, celiac disease, and longevity. We continue to work busily at the Clinic and to recruit volunteers into these and other studies. If you, your family, friends or neighbors are interested in possibly volunteering, please feel free to spread the word and to have them contact us.

My staff and I would like to thank you and your family for your valuable time and dedication to our research. Through our research, we have helped numerous people to improve their health and thus the quality and quantity of their lives. In addition, your participation will one day lead to the genetic discoveries that will pave the way to new preventions, treatments, and even cures for these common disorders. We look forward to serving the Amish community for years to come and wish you and your family health and happiness during this fall season.

- Alan Shuldiner, M.D.
- Elizabeth Streeten, M.D.
- Dan McBride, Ph.D.
- Braxton Mitchell, Jr., Ph.D.
- Richard Horenstein, M.D.
- Soren Snitker, M.D., Ph.D.
- John Sorkin M.D.
- Wendy Post, M.D.
- Nanette Steinle, M.D.
- Scott Hines, M.D.
- Heidi Karon, M.D.
- Mary Morrissey, R.N.
- Janet Reedy, R.N.
- Theresa Roomet, R.N.
- Mary McLane, R.N.
- Marian Metzler, R.N.
- Yvonne Rohrer, R.N.
- Donna Trubiano, R.N.
- Sue Shaub, R.N.
- Nancy Weitzel, L.P.N.
- Sylvia Newcomer
- Shawn Hendrickson
- Patrick Donnelly, R.D.C.S.
- Anita Martinez, R.D.C.S.
- Maryann Drolet
- Rhea Cosentino
- Sarah Raush

Great News! The Amish Research Clinic is moving to 1861 William Penn Way, Lancaster (near COSTCO). We have outgrown our current residence and need a new home that gives us room to grow. We are grateful to Dr. and Mrs. Morton for their hospitality and will continue our working relationship with them. We hope to move before Christmas. Looking forward to seeing all of you at our "Open House".





## Amish Family Hypertension Study

Hypertension or high blood pressure is a common disorder that predisposes people to heart and kidney disease and stroke. As a result of our research in the Amish, we have located a region on chromosome 2 that harbors a blood pressure gene. Dr. Nanette Steinle at the University of Maryland has received a grant to use state-of-the-art laboratory methods to identify the blood pressure gene on chromosome 2. We have made significant progress mapping this gene and are particularly excited about our recent results. Understanding hypertension genes will help to treat and prevent heart and kidney disease and strokes in millions of people. We thank you for your participation in this important study. Please feel free to tell others who may have hypertension about our study and have them contact us if they wish to participate.

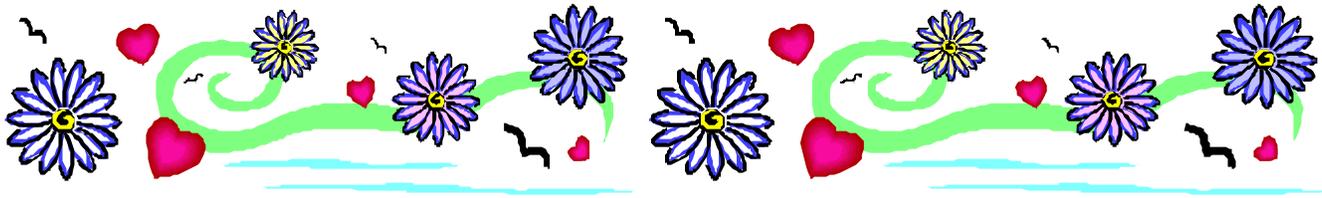
## Amish Family Diabetes Study

Diabetes is a disease in which the level of sugar in the blood is elevated. This can lead to eye, kidney, nerve, and blood vessel problems. The Diabetes Study began in February 1995 to identify genes that predispose to diabetes. To date, we have seen over 1400 Amish volunteers, and have helped over 200 diabetic subjects to better understand and take control of their diabetes. Recruitment continues, so please feel free to contact us or have others contact us if they think they may have diabetes and want to be tested. In the laboratory we have identified regions on chromosomes 1, 10, 14, 15, and 18 that are likely to contain diabetes genes. We are working with several other research groups around the world to find the diabetes gene on chromosome 1. It is our hope that these new discoveries will lead to better medications for patients with diabetes and also allow us to identify individuals at risk for the disease so that it can be delayed or prevented.

## The Sitosterol Study

Sitosterolemia is a rare disease in which levels of plant cholesterol (sterols) in the blood are very high. High plant sterol levels can lead to early heart disease and death, sometimes in childhood. Individuals with sitosterolemia have changes in both (two) copies of a gene that otherwise effectively controls plant sterol levels in the body. The Amish Family Sitosterol Study was started in 2003 to help us compare levels of plant sterols in individuals who have zero or one copy of the changed sterol transporter gene. To date, over 304 Amish volunteers have provided blood samples to help us search for answers. Our findings suggest that individuals with one copy of the changed sterol transporter gene are not at increased risk for heart disease. We hope that knowledge learned from this study will provide new insight into the relationship between fasting blood plant sterol levels and heart disease. We thank those who have volunteered to participate in this study.





## Amish Childhood Obesity Study

Overweight and obesity has become an increasing health concern over the past several years. Excess body weight is associated with problems such as diabetes, heart disease, some cancers and arthritis. Our earlier studies found that although the frequency of overweight and obesity in the Amish are similar to the general U.S. white population, the frequency of adult (type 2) diabetes is about one-half that of the general U.S. white population. This has led us to wonder about obesity rates in Amish children. We suspect that childhood obesity is much less common in the Amish than in the general U.S. white population. The Childhood Obesity Study is designed to gather exact information about activity (by wearing an activity monitor), eating habits (by a questionnaire) and health parameters (blood pressure, weight, waist measurement, height) in Amish children, aged 8-17. Gathering this information will not only help us understand how good eating habits and activity can prevent obesity in children but also serve as information to you about your children's growth and development. All family members ages 8 and above are eligible. Children ages 8 to 13 will receive a book for their participation and all participants, 14 and over, will receive a book or \$10.00. We have enrolled 67 participants to date. Our initial results indicate that indeed Amish children have lower rates of overweight and obesity than general U.S. white children. We would like to thank all of you who have participated thus far in this study. Please call Theresa Roomet at 717-687-8371 at The Amish Research Clinic if your family is interested.



## Amish Family Osteoporosis Study

The Osteoporosis Research Clinic was established in March 1997 to identify genes that predispose to osteoporosis (weak bones). Osteoporosis is responsible for hip fractures in older people and can cause loss of height and chronic back pain and other complications. Identification of osteoporosis genes may lead to better medications for patients with osteoporosis and also allow us to identify individuals at risk for the disease so that it can be delayed or prevented. With your help, we are well on our way toward meeting our goals. Since the Osteoporosis Research Clinic opened, we have seen over 1532 Amish volunteers. We have found that different genes are important for bone strength in men and women and have identified several areas in the genetic material (on chromosomes) where there are genes important for bone health. The next step is to look more closely at these areas to try to identify new genes for osteoporosis. We thank each and every one of you for your participation.

## Amish Family Longevity Study

The goal of this study is to identify genes that allow for a long productive life and to understand what these genes do. To date, 17 Amish men and 13 Amish women aged 90 years or older have participated, as well as 177 of their children, and 125 of the children's spouses. In the course of the study, a number of individuals have been found to have medical problems such as high blood pressure or high cholesterol levels. We were able to improve the health of these individuals through diagnosis and referral to local doctors for treatment. We hope that the letters we sent you about your health status have helped you remain well. Above all, we would like to thank everyone who has participated in the study.



## Amish Family Calcification Study

The Amish Family Calcification Study was designed to test whether heart disease runs in families and whether people with osteoporosis are also at high risk for heart disease. We are measuring the amount of calcium present in the blood vessels of the heart using a special x-ray, called EBCT. EBCT can detect heart disease in its early stages and can be used to identify people at risk for heart disease so that measures can be taken to prevent heart attacks. Over 808 Amish subjects have participated so far. Analysis of the information collected indicates that people with calcification in their blood vessels tend to have higher blood pressures and levels of cholesterol than people without calcification. We have also learned that the amount of calcification people have does tend to run in families. Thanks for your participation in this study.

## Amish Family Celiac Study

Currently, we are completing a study to identify people (and families) with celiac disease to search for genes that predispose to this disease. Celiac disease is a disease of the small intestine caused by an allergic reaction to gluten, a substance found in foods made from wheat, barley, rye, oats, and spelt. Children and adults with celiac disease can have symptoms that include diarrhea or constipation, weight loss, weakness, abdominal pain, vomiting, bloating, loss of appetite, anemia (low blood count) and osteoporosis (weak bones). Often, symptoms can be mild and the disease may not be diagnosed. Treatment with a diet free of gluten results in a dramatic improvement in symptoms. We test for celiac disease with a questionnaire and a simple blood test. We have found that celiac disease is present in the Amish and through this study have diagnosed and improved the health of 123 Amish individuals. Now that we know that celiac disease is present in the Amish community, we will apply for new funding to continue our work. If you have any of the symptoms listed above and would be willing to participate in future celiac disease research, please contact us in writing or by telephone at 717-687-8371 at The Amish Research Clinic.



## **HAPI Heart Study**

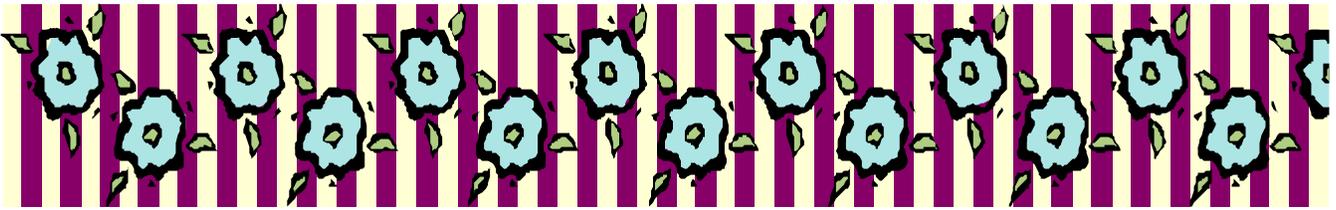
This study is designed to identify how genes interact with various lifestyles factors to influence heart disease. To date, over 884 Amish volunteers have participated in this study. So far we have found that people respond very differently to the same stressor (immersion of the hand into ice water) and diets (high and low salt, and high fat). This is likely due to the effects of inherited factors that differ between people. In the laboratory, we are working to pinpoint these genetic factors so that we can understand better these differences, which may one day lead to new ways to prevent or treat heart disease.

## **A NEW STUDY—The PAPI Study**

The HAPI Heart Study was so successful that we have begun a second study called the PAPI Study. PAPI stands for "Pharmacogenomics of Anti-platelet Intervention". Beginning in August 2006, we will be inviting HAPI Heart volunteers and their family members to participate. The main goal of the study is to understand why some people do not respond to a commonly used medication to prevent heart attacks called clopidogrel (Plavix). This 8-day study involves taking clopidogrel and having blood samples tested to see how well the medication prevents the blood from clotting. PAPI participants will also get free testing for heart problems, high cholesterol, liver, kidney, or thyroid problems, and monetary compensation for their time and effort. We hope you will be willing to participate in this new and exciting study!

## **Women's Breast Health Study**

After skin cancer, breast cancer is the most frequently diagnosed cancer in women in the United States. Because virtually all breast cancers develop in the dense tissue of the breast (not the fatty tissue), women who have unusually dense breasts for their age are at an increased risk of breast cancer. The amount of dense tissue (or glands and ligaments) in the female breast is referred to as breast density and can be easily measured from a routine mammogram (or x-ray of the breast to detect unsuspected breast cancer). We recently completed a pilot study to determine if breast density is heritable in the Amish. Over 300 Amish women and their sisters participated in this study and received a free mammogram. Initial analyses suggest that breast density is highly heritable in the Amish, as it is in other populations. For example, genes appear to account for over 40% of the differences in breast density between women who are of similar age and body size. Encouraged by these findings, we recently applied for a grant to extend this study (by recruiting more volunteers) in order to begin searching for the genes linked to breast density. Lessons learned from this kind of research may improve our understanding of how genes influence breast density and ultimately breast cancer. We thank the women and families who generously gave their time to participate in our pilot study.



## **More findings from our studies...**

### **Does bone health run in families in the Amish?**

Yes! The density (thickness) of the hip and spine is a good predictor of fracture risk in later life. In the Amish, as in other populations, the thickness of the bones is much more similar among people from the same family than among people from different families. This may be because people from the same family are more likely to eat the same diet and to exercise the same amount, or it may be because the genes that people inherit largely determine bone thickness. Most likely, it is a combination of both of these two possibilities. Our preliminary analyses suggest that some of the genes that influence variation in bone density may be on chromosomes 7 and 14.

### **Do the Amish have a lot of calcium in the walls of their coronary blood vessels?**

The amount of calcium in the blood vessel walls of the heart is a predictor of having a heart attack in the future. Some of the factors that prevent people from getting these calcium deposits include physical activity, eating a balanced diet, avoiding smoking, and having low blood pressure and cholesterol levels. We wondered if the Amish would have more or less calcium deposited compared to other populations. With our collaborators at University of Michigan, we compared calcium levels in the heart in the Amish with levels from a population of adults from Minnesota, in whom calcium levels had been measured in the same way. We learned that calcium levels were about the same in the two groups of people, although we would have expected the Amish to have lower levels because Amish tend to be more active and smoke less. There may be other lifestyle differences between the two groups that explain this result.

### **Search for Diabetes Genes**

Adult onset or type 2 diabetes is caused by the interaction of several genes with an unhealthy lifestyle. Studies in people from Iceland suggested that a specific gene called TCF7L2 might be involved in the development of diabetes. Other studies in Finns and Jewish people found another gene called HNF4A that might be involved in diabetes. Our studies in the Amish have confirmed both of these findings and were among the first studies to be published that replicate these important discoveries. We have recently completed the testing of over 100,000 different markers from genetic material of our Amish Family Diabetes Study participants and have identified several regions of the genome that are likely to harbor other diabetes genes. We are very excited by these recent developments and look forward to discoveries that will lead to prevention and new treatments for diabetes.

### **Are diabetes and osteoporosis (weak bones) more common in the Amish?**

No! In fact, our studies show the opposite. For adult (type 2) diabetes, the frequency in the Amish is only about one-half that of the general U.S. white population. Similarly, we found that the frequency of hip fractures that occur in the Amish is significantly lower than in the general U.S. white population. Protection from diabetes and hip fractures may be because the Amish are more physically active, which is known to have beneficial effects on these two diseases.

### **Are there differences in how long it takes people to clear fat from their blood-streams?**

When we gave people a milkshake to drink containing a large amount of fat and measured the amount of fat in their blood for several hours afterward, we learned that there are differences in how long the extra fat (measured as triglycerides) stays in the bloodstream and how high the level of fat gets in the bloodstream. This is true even among people with similar amounts of fat in their blood before they drink the shake. We learned that a portion of the change in blood fat appears to result from genetic factors, and we have started to identify some of the gene changes that may be responsible. Since people at risk for heart disease tend to be the same people who take a long time to clear fat out of their blood, knowing these genes will likely help us to better understand causes of heart disease and ways to treat and/or prevent it.

