2020 Annual Newsletter

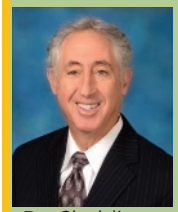
Amish Research Clinic

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

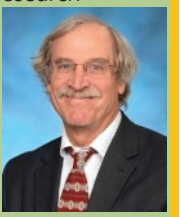
Greetings from the Amish Research Clinic

We hope you and your family are healthy and happy in these difficult and challenging times. Due to the COVID-19 pandemic, in Mid-March we suspended all field work and research activities. We think this is very important for the protection of community members as well as our own staff. We will start back up after we receive word that it is safe to do so. In this newsletter, we have included an information page (pg. 13) about the coronavirus that you may find helpful. Please stay updated with trusted information by reading your local newspaper or calling the Pennsylvania Department of Health at 1-877-PA-HEALTH.

During this pause in Clinic activities, we took the opportunity to send out our annual newsletter a bit early to keep you informed about our medical research and what we have learned from the studies you have made possible by donating your precious time and effort as a research participant. This is a special year for us as it marks the 25th anniversary of the opening of the Amish Research Clinic in 1995! We hope you enjoy Dr. Shuldiner's reflections on the history of the Clinic.



Dr. Shuldiner



Dr. Mitchell

The story of the beginning of the Amish Research Clinic: Reflections on 25 years of continuous service to the Amish community through research

Alan Shuldiner, MD

It was 1993. I met Dr. David Marsh, an accomplished researcher at Johns Hopkins who was studying genes for asthma in the Amish. This is when the light bulb went off in my head. Why not use the same approach to identify genes for blood sugar levels and diabetes? I contacted Dr. Victor McKusick, a senior faculty member and an international icon in human genetics, having identified and characterized dozens of genetic diseases among the Amish. He was quite encouraging and arranged for me to visit Sadie Beiler, an Amish liaison who worked with the Hopkins team.

The defining day in my career (and life) came one cold fall day when I first met Sadie. I told her I was interested in studying diabetes in the Amish. Her first words, still etched in my mind today, "Oh, I have diabetes and you know, in the Amish, diabetes runs in families!" We quickly developed a plan to go to all of Sadie's 11 brothers and sisters and test them for diabetes. We would also visit several Amish who Sadie knew had diabetes, to test them and their family members as well.

For two days each week, I'd awaken in Columbia, Maryland by 3 AM to arrive at Sadie's no later than 5 AM. I'd pick up Sadie in my Honda Accord, and she brought me to an Amish home where we performed oral glucose tolerance testing. Once testing was completed, my hatchback turned into a mobile lab, usually in the participant's driveway. I'd fire up a gas generator, process the blood, and freeze it in a dry ice chest before returning to Baltimore where sugar levels were measured in the lab. I have so many memories of my drives with Sadie; her wise words and sayings, interactions with her family members and other research volunteers, and the winter of 1996 in which ice storms coated the roads and driveways with inches of snow and ice making our field work quite challenging.

One day, Sadie introduced me to her neighbors, David and Naomi Esh, who had a lot of diabetes in their family. Before I could blink an eye, a family gathering was arranged and, in one very long evening, we performed more than 20 glucose tolerance tests. This introduction resulted in a lasting friendship with the Esh family that transcended the diabetes study and all other studies since.

Over the course of those two years, we made many new diagnoses of diabetes. With each new diagnosis, I would provide a glucose monitor and strips to newly diagnosed research participants with instructions on diet, exercise, weight loss, blood sugar monitoring, and when necessary, referral to one of the local doctors for further treatment. While telling someone for the first time that they had diabetes was not my favorite activity, providing this information along with advice regarding blood sugar monitoring and treatment was one of the most rewarding parts of this work. I knew that early diagnosis and treatment of diabetes could prevent or delay some of the devastating complications of diabetes such as kidney failure and eye problems.

Soon after initiating the diabetes study, I obtained funding to expand the project. We would recruit hundreds of Amish research participants and test them for diabetes. This would be, by far, the largest study ever conducted in the Amish and most, including Sadie, thought I was crazy! We would require significant infrastructure including a clinic with a laboratory, van for field work, and dedicated staff. I connected with Dr. Holmes Morton at the Clinic for Special Children. We were classmates together at Harvard Medical School. He offered the first floor of the Clinic for Special Children and the Amish Research Clinic was born. We opened on February 14, 1995 – Valentine's day – and have been in continuous operation ever since. We performed glucose tolerance tests each day on 6-8 volunteers and, within 3 years, had recruited the planned number of subjects and more. The success of the diabetes project led to dozens of new projects to study osteo-porosis, heart disease, aging and longevity, and how people respond to medications like aspirin and Plavix, among many other studies shown in the timeline.

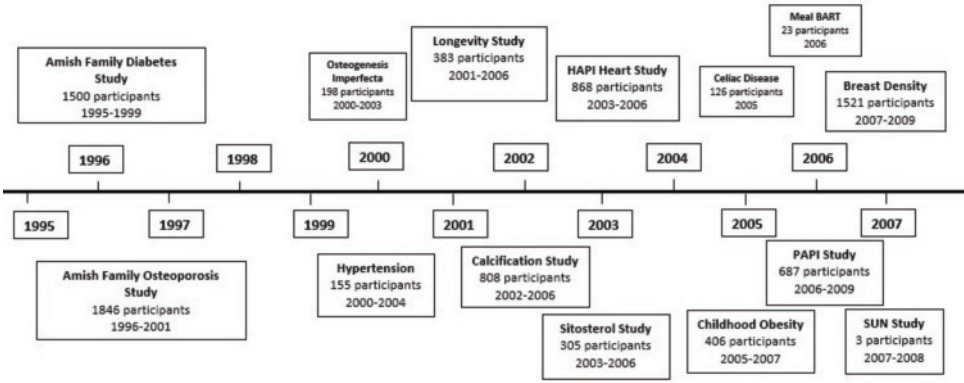
By 2007, the Amish Research Clinic outgrew the first floor of the Clinic for Special Children and we moved to a larger building at the Greenfield Industrial park. In 2010, we began the Wellness study, which is now our largest study having recruited more than 7000 Amish volunteers. In 2015, we moved to yet a larger facility in Lampeter, which is our home for the indefinite future.

Really important scientific findings, almost too numerous to mention have been published over the years which have had a major impact on health in the Amish community and worldwide. Updates on these projects are provided in this newsletter.

Thanks to the Amish community and an amazing staff, the Amish Research Clinic is conducting additional studies based on findings from our earlier studies. We expect to continue our service to the community through research for many years to come.

Amish Research Clinic Team:

Susan Shaub, BSN, RN
Maryann Drolet, BSMT, ASCP
Donna Trubiano, RN
Dawn Fox, RN
Mary McLane, MSN, CNM
Diane Montgomery, BSN, RN
M. Ranea Riehl, RN
Nancy Weitzel, LPN
Sylvia Newcomer, BSMT, ASCP
Karen Howk, BSMT
Patrick Donnelly, RDCS
Tracy Broderick
Grace Redcay
Gina Guaraldi
Fred Young
Robert Henry
Elizabeth Zehr



Amish Family Diabetes Study – Searching for genes involved in the development of type 2 (adult-onset) diabetes.

Osteogenesis Imperfecta – Studying a large Amish Family with a genetic change that causes "Brittle Bone Disease".

Hypertension – Looking for genes involved in the development of high blood pressure.

Longevity Study – Studying the genetics of people over 90 years of age and their 1st degree family members.

Calcification Study – Looking for genes that influence the levels of calcium found in coronary arteries and a person's susceptibility to heart disease.

HAPI Heart Study – Studying how specific environmental factors interact with genes to influence risk for heart disease.

Sitosterol Study – Studying a gene change that affects how the body processes plant-based cholesterol.

Celiac Disease – Studying Amish with gluten allergy.

Childhood Obesity – Study of the prevalence and risk factors for obesity in Amish children and comparison to children in the general population.

Meal BART Study – Study of how fat in the diet affects the function of blood vessels.

PAPI Study – Discovery of gene changes that interfere with a person's response to a blood thinning medication (clopidogrel or Plavix).

Breast Density Study – Study of the relationship between breast density measured by mammogram, breast cancer and genes.

Amish Sunshine Study - A study in which we evaluated differences in how well people make Vitamin D in their bodies after a sunlamp exposure to the skin.

Sitosterol Bench to Bedside – Studying how sitosterol in the diet affects blood lipid (fat) levels and other blood levels involved in heart disease in participants with and without a gene change that increases blood sitosterol levels.

Staph Aureus Study – A study of how common methicillin resistant Staph Aureus is in the Amish population.

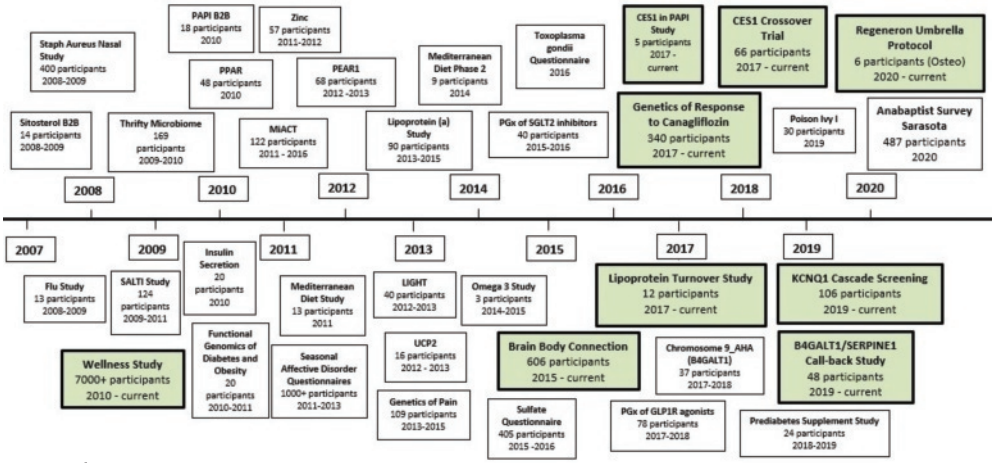
Flu Study – A study to better understand why older people do not respond as well to the flu vaccine compared to younger people.

SALTI Study – Studying individuals with a gene change involved in kidney salt transport to understand its effects on salt loading, blood pressure, and the use of thiazide diuretics.

Microbiome – Studying gut microbes in Amish with obesity and metabolic syndrome.

PAPI Bench to Bedside – Exploring why some people respond more than others to differing doses of the blood thinner, clopidogrel.

PPAR - Searching for genes that determine a person's response to pioglitazone, a medication used to treat diabetes.



Insulin Secretion – Determining the effect of gene changes on a person's response to certain diabetes medications.

Zinc - A study of the effect zinc supplementation on insulin secretion in subjects with and without a common genetic variant in SLC30A8, a zinc transporter present in the pancreas.

MiACT - Studying how a gene change in APOC3 affects how fat is metabolized by the body.

Mediterranean Diet Study – Studying the effects of a Mediterranean diet and dietary fiber on the composition and function of the gut microbiome.

Functional Genomics of Diabetes and Obesity – Study to identify differences in how genes are expressed in fat and muscle of people with diabetes and obesity.

PEAR1 Study - Examining the effect of variations in the PEAR1 gene on a person's response to increasing doses of aspirin.

Lipoprotein (a) – Using MRI to study genetic changes that affect Lp(a) levels and their link to hardening of the arteries.

Light Study – Wearing light monitors to measure the amount and type of light that Amish people are exposed to during the course of the day.

Seasonal Affective Disorder – Studying depression that occurs during the winter months.

UCP2 Study - Investigating why people with pre-diabetes or diabetes respond differently to atenolol, a medication for high blood pressure.

Genetics of Pain – Studying the link between genetics and pain.

Omega 3 Study – Investigating the effects of omega-3 fish oil on people with metabolic syndrome.

T. Gondii questionnaire study – A study to determine the prevalence of exposure to T. Gondii, a pathogen that can cause toxoplasmosis.

Pharmacogenetics of SGLT2 inhibitors – Studying response to canagliflozin, a medication for diabetes, in healthy, nondiabetic people with certain genetic changes.

Sulfate Questionnaire – Using social responsiveness questionnaires to investigate whether there is any connection between sulfate deficiency and autism.

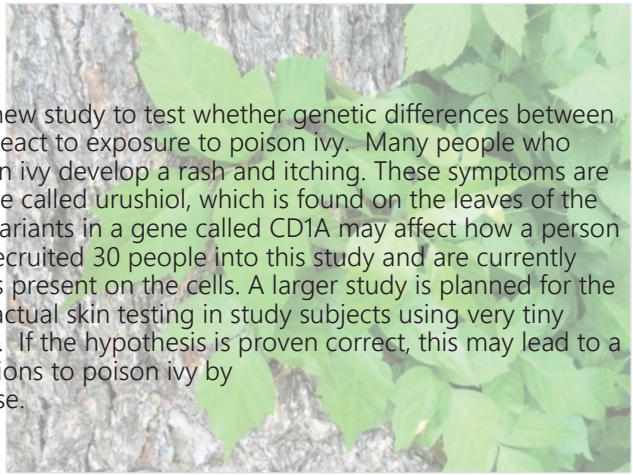
Chromosome 9_AHA – Preliminary study of cholesterol levels and blood clotting in people with and without a variation in the B4GALT1 gene.

Pharmacogenetics of GLP1R agonists – Studying healthy, non-diabetic people for genetic changes associated with differing responses to exenatide and sitagliptin, two FDA approved medications used by diabetics.

Prediabetes Supplement Study – Study the impact of a dietary supplement taken by prediabetic adults on pre-diabetes blood markers.

New Studies

Poison Ivy Study



We have started an exciting new study to test whether genetic differences between people may affect how they react to exposure to poison ivy. Many people who come into contact with poison ivy develop a rash and itching. These symptoms are a reaction to an oily substance called urushiol, which is found on the leaves of the plant. We hypothesize that variants in a gene called CD1A may affect how a person reacts to urushiol. We have recruited 30 people into this study and are currently examining how much CD1A is present on the cells. A larger study is planned for the fall in which we will perform actual skin testing in study subjects using very tiny controlled amounts of the oil. If the hypothesis is proven correct, this may lead to a new therapy to prevent reactions to poison ivy by subduing this allergic response.

Lyme Disease

We mailed a questionnaire about Lyme Disease to 500 members of the Amish community to seek information about exposures, diagnoses, and concerns about this disease. Based on these responses and overall concerns expressed in the community, we have included Lyme Disease as one of the topics for the 3rd Annual Amish Health Conference that has been rescheduled for October 2, 2020.

Umbrella Study

In collaboration with the Regeneron Genetics Center, analyses of the genetic results in over 6,000 Amish participants have revealed multiple gene variants (changes) that appear to affect disease risk. This new study will help us understand how these variants affect health. Currently, we wish to more deeply study six gene variants that appear to improve health and lower an individual's risk of disease. The knowledge we gain may help us create new medications that mimic the health effects of these variants in people who are at increased risk of disease.

Osteoporosis Study

This study is one of our longest running studies, started in March of 1997. In collaboration with many other groups around the world and thanks to our many wonderful Amish participants, we have found 60 genes that are important for bone health. We are excited to be able to enroll new study participants so that we can study a genetic change that has an impact on bone strength. If you are on our recruitment list, we hope you will help us learn more about this gene change by joining the study when you are approached by our study team. We are continuing to offer a free DXA bone density scan to those who have been identified with low bone density through the Wellness screening and as 2-year follow-up to previous enrollees diagnosed with osteoporosis.

GAL-B4GALT1 & Serpine Call-back Study

High cholesterol (LDL) is a major risk factor for heart disease, the leading cause of death worldwide. LDL level is governed by genetics and environmental factors. We recently discovered a strong new association between a variant (change) in the B4GALT1 gene and low levels of LDL in the Old Order Amish. The purpose of this study is to better understand how this variant works by comparing Amish individuals with and without the variant. The knowledge gained from this study may lead to the discovery of new medications to combat high cholesterol.

This study has two parts that involve people with and without the gene change. Part A involves sending health questionnaires to previous Amish Research Clinic participants. Many of you may have received questionnaires in the mail in December of 2019. If you have not yet returned it to us, you can still help us by answering the questions and returning them to us. Part B involves having specific people visit the Amish Research Clinic for blood tests, an oral glucose tolerance test, EKG, echocardiogram, DXA scan, lung function tests, and some other blood vessel-related tests. If you are on this list, a nurse will visit you to ask if you would like to join the study. Thank you to the many people who have already returned their completed questionnaires or have taken part in the clinic portion of the study.

New Studies, continued

KCNQ1 Cascade Screening Study

This study follows up the KCNQ1 Return of Results Study and is open to the original 88 individuals found to carry the gene change (carriers) and their first-degree family members. Please refer to next page for details about KCNQ1 and LQTS.

The study has two goals. One is to offer a simplified process for family members of carriers to be tested for the gene change by offering free, in-home, saliva-based genetic testing. This is called cascade screening – testing flowing down from known carriers. The second goal is to understand participants' opinions about receiving their genetic results and about the cascade screening process for the KCNQ1 gene change. This information is obtained through response to mailed questionnaires and in-person interviews with some of the participants. Learning about participants' experiences will help us improve the way we present information to people who have genetic variants that need medical follow-up.

Donation Message

The Amish Research Clinic is a nonprofit organization that has been a constant in our community. Freewill donations to help with operating expenses are appreciated. Checks can be made payable to the University of Maryland Baltimore Foundation/Amish Clinic (or UMBF/Amish Clinic), which administers gifts for the University of Maryland Amish Research Clinic. Kindly send your donation to:

University of Maryland School of Medicine
Office of Development
Attn: Traci Morgan
31 South Greene Street, Third Floor
Baltimore, MD 21201

Alternatively, you can donate online at: **medschool.umaryland.edu/Amishgift**

We want to thank those of you who have provided us support in the past. With your help, we have been able to purchase two new transport vans, provide free genetic confirmation and counselling of the KCNQ1 variant to participants, and cover other expenses associated with our clinic. If you have any questions, please call Pamela Lambert at 410.706.0419 or 717.512.6013.

Gifts to support the University of Maryland School of Medicine are administered by the University of Maryland Baltimore Foundation, Inc. A portion of any contribution to the University of Maryland School of Medicine may be used to enhance advancement efforts.

Return of Genetic Results

Sometimes the gene variants that we find are already known to have a significant impact on an individual's health or their risk for disease. In some of these cases, we feel obligated to give people an opportunity to learn about the gene change and to have the result confirmed by a clinical laboratory. Notifying the individual could help with early diagnosis of a health problem, early treatment to decrease health risk, or the potential for lowering medical costs that add up while someone is searching for the cause of health issues. We are currently providing clinical testing and genetic counseling to these individuals at no cost to them, using donated funds. Hopefully, we can continue to do so in the future.

KCNQ1 Return of Results

A variation found in the KCNQ1 gene is one such finding that we have returned to some of our previous participants. This variant causes Long QT Syndrome (LQTS) which affects the electrical activity of the heart and can affect the heart rhythm. This change is measured with an electrocardiogram or EKG. LQTS increases the risk of fainting and sudden death throughout the lifespan, most commonly during physical activity, and causes at least 10% of crib deaths. The KCNQ1 gene variant that causes LQTS was found to be present in 1 out of 45 Amish. Although half of these people never have symptoms and the risk of sudden death is low, we have no way to predict who will experience these. LQTS is treatable with Beta blockers, medications that are very effective in preventing fainting and sudden death by 70-90%. They are generally safe and do not cause side-effects in 95% of people who take them.

This variation was originally found in 135 previous participants. They were contacted by letter and offered the opportunity to have the return of genetic results as described previously. 88 people accepted the offer, were clinically tested, received genetic counseling and were referred to follow-up with their physician. Since first-degree, blood-related family members (parents, siblings, and children) each have a 50% chance of having the KCNQ1 variant, we encouraged the participants to share this information with their family, so they could decide about getting tested. Genetic testing is available through the Clinic for Special Children.

Ongoing Studies

Amish Wellness Study

We have started to study the information collected in the Wellness Study and found that Amish appear to be less than half as likely to have diabetes or high blood pressure and slightly less likely to have high cholesterol compared to non-Amish. These differences are impressive. We believe that higher physical activity, stronger social relationships, or other aspects of the Amish lifestyle may help protect against these diseases.

We have suspended recruitment for the Amish Wellness Study due to current concerns about COVID-19 (coronavirus) risk. This study (which is funded by our partnership with the Regeneron Genetics Center LLC) offers all Amish adults basic wellness screening including tests of cholesterol, blood sugar, thyroid, bone strength, and heart health. Blood is also being collected and stored at the University of Maryland for research on genetic and non-genetic factors in health and disease. When we are able to resume the Wellness Study, we plan to visit the remaining Church districts which have not yet participated, and we are also seeking funding to expand a version of the study into other Old Order Amish and Mennonite communities.

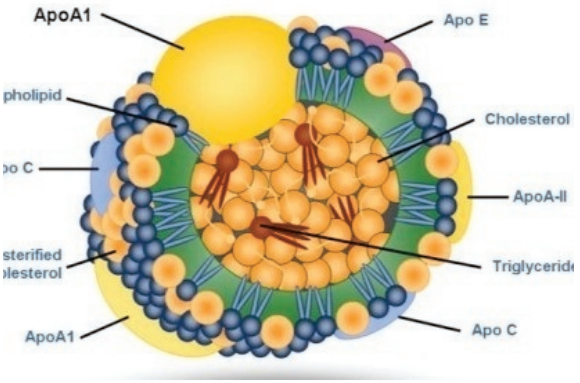
CES1 Study

Currently, there are several drugs that can be used when a person has a heart attack. Most of these drugs help prevent future heart attacks in the same way (by thinning the blood); however, they perform their actions in slightly different ways. Today, most people receive a drug called clopidogrel (also known as Plavix) because it generally works well and is cheaper than other medications. However, clopidogrel doesn't work well in a subset people due to many factors, one of which is genetics. Therefore, it would be helpful for doctors to know when it is a good idea to give someone clopidogrel vs. a different drug. Another drug that could be used is called ticagrelor. In this study, we are studying whether or not genetic differences in a gene called carboxylesterase 1 (CES1) causes changes in how people respond to clopidogrel. Also, we would like to see how the same person would respond to ticagrelor. By performing this study, we hope to be able to prevent heart attacks or other complications in some people in the future by giving them the drug that works best for them based on their genetic make-up.

Genetics of Response to Canagliflozin (GRC) Study

Medications do not work the same way for everybody. This can be due to differences in genes. Canagliflozin is an FDA approved drug that is used to treat type 2 diabetes. This study measures the effect of canagliflozin on healthy, non-diabetic people to see if a person's genes influence how well it removes sugar from the blood. We also want to see if a person's genes influence whether they experience side effects from the drug. This information may help doctors to choose the best medication or best dosage for someone with type 2 diabetes. Please call the Amish Research Clinic if you would be interested in participating in this study.

Lipoprotein Turnover Study



Lipoproteins are special types of packages in the blood that help carry and deliver dietary fats and cholesterol to parts of our body that need them. In this study we have compared siblings with and without a genetic change that affects how the body makes or uses lipoproteins. We are looking at the way these fat and cholesterol packages are made and broken down. This information might help develop new ways to prevent or treat disorders of fat and cholesterol metabolism.

University of Maryland Team:

Alan Shuldiner, MD
Amber Beitelshees, Pharm. D., MPH
Braxton Mitchell, PhD, MPH
Christy Chang, PhD
Coleen Damcott, PhD
Elizabeth Streeten, MD
Elliot Hong, MD
Jeff O'Connell, DPhil.
Joshua Lewis, PhD
Kathy Palmer, BSN, RN
Kristi Silver, MD
Mao Fu, MBBS, PhD
May Montasser, PhD
Michael Miller, MD
Nanette Steinle, MD
Pamela Lambert
Robert Reed, MD
Samantha Lightner
Simeon Taylor, MD
Teodor Postolache, MD
Toni Pollin, PhD

Ongoing Studies, continued

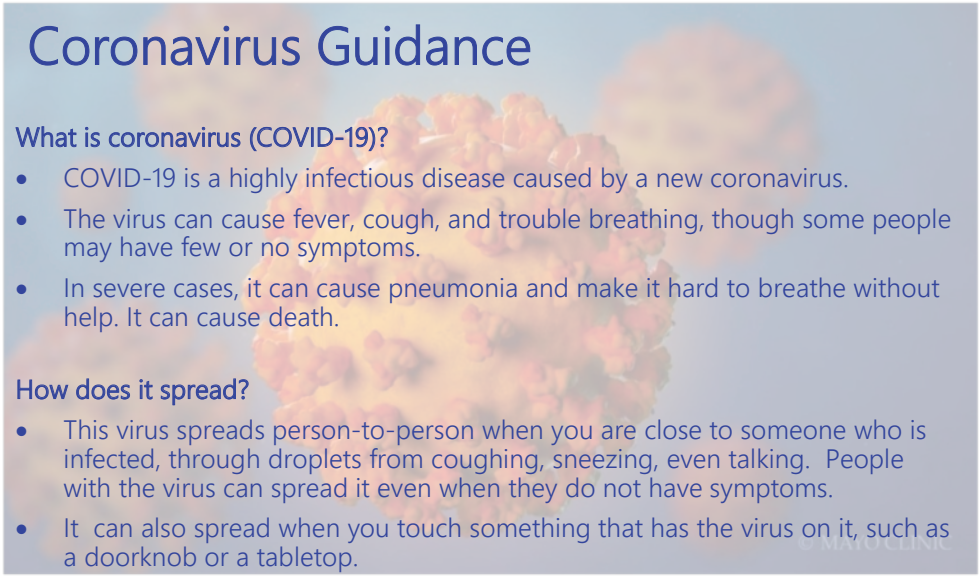
Brain Body Connection Study

The purpose of this research is to find out more about brain differences that make it more likely an individual will have mental health problems. Families with and without individuals who struggle with mental health problems have participated in this 5-year study. Participants completed two full days of testing including a clinical assessment and interviews at the Amish Research Clinic and magnetic resonance imaging (MRI) of the brain in Catonsville, MD. These images are being used to help us better understand the brain circuits, or wirings, which are related to mental health.

Studies from the Amish Research Program have been described in over 316 publications. These can be viewed on this website:

https://www.ncbi.nlm.nih.gov/myncbi/collections/47782571/

Coronavirus Guidance



What is coronavirus (COVID-19)?

- COVID-19 is a highly infectious disease caused by a new coronavirus.
- The virus can cause fever, cough, and trouble breathing, though some people may have few or no symptoms.
- In severe cases, it can cause pneumonia and make it hard to breathe without help. It can cause death.

How does it spread?

- This virus spreads person-to-person when you are close to someone who is infected, through droplets from coughing, sneezing, even talking. People with the virus can spread it even when they do not have symptoms.
- It can also spread when you touch something that has the virus on it, such as a doorknob or a tabletop.

The best ways to prevent the virus are:

- Stay at home unless you need food, medicine, or other essentials; cover your nose and mouth with a mask or scarf if you must go out.
- Wash your hands often with soap and water for 20 seconds. If soap and water aren't available, use an alcohol-based hand sanitizer.
- Avoid groups and try to stay at least 6 feet away from people outside your household.
- Avoid touching your mouth, nose, and eyes with unwashed hands.
- Cover your mouth with a tissue when you cough or sneeze. Then throw the tissue in the trash and wash your hands. Or cough or sneeze into the crook of your arm, then wash.
- Use a disinfecting cleaner to clean things that you touch often.

If you are sick:

- Stay at home and away from others, including family.
- Call your doctor. If you don't have a doctor, you can call Penn Medicine's toll-free COVID-19 hotline at 1-833-983-1350 with questions.
- Call 911 if you have severe trouble breathing or another medical emergency.

Stay updated with trusted information. Read your local newspaper or call the Pennsylvania Department of Health at 1-877-PA-HEALTH.

A research study is under consideration involving members of the Amish community who were confirmed or suspected to have contracted the virus. If you meet this criteria and may be interested in participating, please leave us a message with your name, age, and phone number at 717-392-4948.

Locations of the Amish Research Clinic

The Clinic for Special Children

Strasburg, PA

1995—2007

1861 William Penn Way Lancaster, PA

2007—2015

921 Village Road

Lampeter, PA

2007—current

3rd Annual Health Education Conference for the Plain Community

Rescheduled for
October 2, 2020
in Intercourse, PA

Presented by the University of Maryland School of Medicine

Amish Research Clinic

Space is limited and Registration will be required

This day-long program is free and will include information about

- **Celiac disease**
- **Immunizations**

and

- **Lyme disease**

Each topic will feature speaker presentations and panel discussion to address questions.

Speakers & Panelists are from the Clinic for Special Children, Parochial Wellness Centers, Wellspan Health, Central Pennsylvania Clinic, the University of Maryland, Harvard Partners and Regeneron Genetics Center.

For more information or to register, call the Amish Research Clinic:

717-392-4948

A R C Amish Liaison Team:

Naomi Esh	Mary Stoltzfus	Anna Esh
Barbie Stoltzfus	Lydia Zook	Esther Smucker
Fannie Stoltzfus	Verna Petersheim	Barbie Beiler
Hanna King	Sylvia King	Marian Stoltzfus
Susie Fisher	Barb Stoltzfus	Katie King
	Susie Stoltzfus	

University of Maryland
School of Medicine
Amish Research Clinic
921 Village Road
Lancaster, Pa 17602

Phone #: (717)392-4948

Our Mission

The Amish Research Clinic contributes to improvements in healthcare through research. We serve as a resource for health information and knowledge to the Amish Community.