

### The future of the Strong Heart Study

The Strong Heart Study (SHS) has been going since 1989 with a focus on cardiovascular diseases, (heart, stroke, and blood vessels) especially in persons with diabetes. SHS receives funding from the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health, and the funding is



awarded in 4-5 year periods. In the near future, the investigators will request permission to apply for support of the next phase of SHS. Strong Heart seeks information that will improve care or prevent diseases. Therefore, we are now designing the next phase of SHS with these same principles. We have completed exams of our family two members that used ultrasound to look at the heart, and also the neck and leg vessels. We propose to do one more exam, but this time we would likely study different things.

We have learned from our results, and other scientists have also proposed, that fat accumulated in the liver may play a key role in both diabetes and diabetic heart disease. Therefore, we will seek funding to do an MRI scan (painless, no radiation pictures) of the abdomen that will allow us to measure fat in the liver. We believe this will lead to better understanding of what leads to high blood sugar and blood fats, and therefore, how to prevent and treat them. In this exam, we also hope to perform a short test to learn more about what controls blood pressure. This test, called the 'cold pressor' test, will take blood pressure measurements before and after a person's arm is dipped into cold water for three minutes. We will use a special machine to take the blood pressure that gives much more information on how the blood is flowing in the vessels. We believe this will give information on why blood pressure goes up in some people and how to get blood pressure medications to work better. The Strong Heart Study staff at each field site will be seeking community permission for our application, and we welcome your questions and suggestions.

## SANDS has worldwide impact

We recently reported to you that the SANDS trial ("Stop Atherosclerosis in Native Diabetics Study") showed that treating to lower targets for LDL (the bad cholesterol) and blood pressure in Indian men and women with diabetes seemed to reduce the build up of fat in the arteries and improve heart function. This trial was noteworthy because of the outstanding performance of our participants and staff, and because it developed stepwise treatments for LDL and blood pressure that can be applied successfully by providers in Indian country. Recently, SANDS also received national and international attention because of its quality, and because it is now the only study that provides information on the effectiveness of a medicine for lowering cholesterol that is often used in addition to statins. This demonstrates that studies like Strong Heart and SANDS in Indian communities have double value; they are designed to learn about ways to prevent and treat heart disease and its risk factors in American Indians, but the results we publish have been helpful in many other populations, as well. Because diabetes and heart disease are now common throughout the U.S. and the world, the information gained from SANDS is helping people across the globe.

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### Stroke rate high in American Indians

Researchers in the Strong Heart Study recently found troubling information about strokes in American Indians. The SHS data show that American Indians are more likely than white or black populations in the U.S. to experience a stroke in their lifetime, and American Indians are more likely to experience a stroke at a younger age. In addition, the death rate for those experiencing their first stroke is higher in American Indians than in white or black populations in the U.S. This study was the first to provide data about strokes in American Indians and the risk factors that contribute to strokes.

There are two types of stroke: ischemic stroke and hemorrhagic stroke. Ischemic stroke, the most common type of stroke, occurs when a blood

vessel that supplies oxygen to the brain is blocked. This type of stroke is usually the result of clogged arteries, known as atherosclerosis, which happens when fat, cholesterol, and other substances collect on the walls of the arteries to form plaque. This plaque build-up makes it hard for blood to flow freely through the arteries and can cause a blood clot. The other type of stroke, hemorrhagic stroke, is the result of



bleeding in the brain and is often associated with high blood pressure, but can be caused by other factors, too.

Ischemic stroke accounted for 87% of strokes in this study. On average, participants who suffered a first-time stroke during the study were in their mid-sixties. Eighteen percent of those who suffered from a stroke died within one month, and 32% died within one year. This is 1.5 times the rate of death found in other populations.

This study shows that American Indians are at a great risk for strokes. Researchers have found that certain steps can be taken to prevent strokes, such as controlling blood pressure and blood glucose, and avoiding smoking. In

> addition, this research showed that there is a strong connection between blood pressure, diabetes, stroke and protein in urine. This relationship needs more study.

> We hope our results will lead to further studies that can improve prevention strategies and aid American Indians in preserving their cardiovascular health.

### A new study is coming: Strong Heart Stroke Study

The SHS investigators are working with researchers at the University of Washington in Seattle to initiate a new project called the Strong Heart Stroke Study. We are currently seeking permission from all SHS communities to conduct this project. This study focuses on stroke and other mental problems in the elders.

Strong Heart Study data have shown that stroke rates in American Indians are more than twice that of the U.S. population. Strokes, which involve a lack of proper blood flow to a portion of the brain for a period of time long enough to cause death of brain cells, lead to disability and reduced quality of life. Even "mini strokes" (a temporary interruption of blood flow to the brain) can affect mental and physical function. Life expectancy in American Indians is increasing, but little is known about factors that lead to stroke or reduce quality of physical and mental function.

The Strong Heart Stroke Study will provide invaluable information about stroke in American Indians. We will be able to determine how many people have had "silent" or "mini" strokes (also known as transient ischemic attacks), and then determine the impact that the mini strokes have on subsequent physical or mental functions. This study will also help determine what characteristics, such as blood and physical changes or heart function, may predict strokes among Indian people. In addition, we will be able to evaluate predictors of poor physical or mental function later in life, measure brain changes, and measure the extent of brain damage in those who have had a paralytic stroke.

Participants, currently 65 and above, from the original Strong Heart Study will be asked to participate. Participants will be given a clinical examination that will include physical function, brain function (testing for things such as memory and depression), blood pressure, ECG, blood tests and an MRI of the brain, which will provide



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assessment of previous strokes and stroke-like changes. MRI stands for "magnetic resonance imaging." It is a non-invasive medical test that uses strong magnet and radio waves (like those from a cell phone) to generate a picture of the inside of the body. During the MRI procedure, study personnel will remain in the room with participants who will be able to listen to music during the scan. It is important to note that the MRI does not use radiation.

The Strong Heart Stroke Study will provide information that may be used to develop programs to prevent stroke and identify opportunities for interventions. It will also provide information on predictors of healthy lifestyles among Indian elders. This can lead to programs to increase their quality of life. In addition, this study will provide important information about mental dysfunction

(Alzheimer's disease) among American Indians.

The Strong Heart Study appreciates everyone who has dedicated his or her time to the study, and we look forward t o continued partnership with you in the Strong Heart Stroke Study.



# Strong Heart Study Is Participating in a Multi-Center Study to Assess the Effect of Behavior and Environment on Recent Genetic Findings

Have you ever wondered how relevant the results of genetic studies are to you? The SHS scientists do, too. Over the past few years, more than 200 genetic variants have been reported in scientific journals, as well as in the press, that are associated with diabetes, obesity, cancer, and

other common diseases. These results come from a new approach called genome-wide association (GWAS) where up to one million variations in participants' DNA are used to search the genome to identify which of these variations is associated with disease risk. However, most common diseases such as heart disease have not only genetic, but also environmental and behavioral causes. The Strong Heart Study was asked to participate in a consortium of studies designed to tease out what modifies the extent to which genetic variants, environment, and behavior affect risk for heart disease and stroke in different communities with differing ethnicities and

lifestyles (no results will be linked to SHS individuals or communities).

There are two levels of involvement in this effort. First, the SHS is a member of CALiCo, a consortium with 4 other population-based studies, all with an extensive set of data on their participants, and all designed to identify both genetic and environmental risks for heart disease. This consortium is led by Gerardo Heiss, M.D., Ph.D. at the University of North Carolina, and includes several SHS investigators. CALiCo is part of a larger group of studies, called PAGE, funded through an initiative of the National Human Genome Research Institute. The studies in PAGE total more than eight (including those in CALiCo),

and include Asian American, Black, White, Hispanic American, Native Hawaiian, and because of the SHS's involvement, American Indian participants. The goals of PAGE are to type these recently-identified genetic variants and see how they are related to a person's physical characteristics, such as weight, blood sugar levels, blood pressure, and then how they are affected by behavioral and environmental factors such as medications, smoking, and diet, and ultimately how all of these genetic, biological and behavioral factors interact with one another to affect the severity and risk of disease.

The results of PAGE could increase our ability to identify individuals who are at risk to develop disease because of their genes. However, it should also give clues as to how they might reduce their risk by changing their behavior or altering their environment. This is particularly relevant in communities with high rates of disease, such as those participating in the SHS, since it could lead to identifying lifestyle changes that could have a more immediate effect on reducing risk for and rates of disease.

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#### ADDRESS SERVICE REQUESTED



### Newcomers to SHS

The Strong Heart Study has always been proud of the role we play in encouraging American Indian students and young professionals to become involved with medical research, and many have been involved with us since the beginning of the project. They have become a part of the planning and conduct of the Strong Heart Study and been able to access a wealth of data that they can analyze and write publications to complete advanced degrees, as well as further their careers. In addition, American Indian trainees and investigators have often provided special insight to allow more accurate interpretation of the data; not to mention the enthusiasm they bring to those of us who have been with SHS for a "long" time.



Darren Calhoun, Ph.D., Psychologist and doctoral fellow working with SHS.

We have had several newcomers to SHS recently. They include John Thomas Egan, who is completing his last year in medical school at the Univ. of Minnesota. He has been analyzing some of the SHS data on "locus of control," which is a measure of how much a person believes that their health condition is controlled by themselves, compared to how much is controlled by luck or other people, such as doctors. John's grandfather was a member of the Tlingit tribe in southeastern Alaska.

Dr. Jason Deen, is a second year resident at the University of Minnesota, studying pediatrics and adult medicine. He has begun work looking at the factors that play a role in the development of high blood pressure in young people of the SHS Family Study. Jason is a member of the Blackfeet tribe of Montana.

Dr. Darren Calhoun is a Psychologist who completed his PhD in clinical psychology at the University of Montana and has been awarded a post doctoral fellowship to work with the Strong Heart Study at the Arizona center. A member of the Northern Arapaho Indian Tribe of the Wind River Indian Reservation in Wyoming, Dr. Calhoun's primary research interest has been in the area of behavioral interventions designed to prevent or delay the onset of diabetes, prevent health complications in those persons diagnosed with diabetes, and improve overall management of diabetes among American Indian populations.