



STRONG HEART STUDY

INVESTIGATING CARDIOVASCULAR DISEASE
IN AMERICAN INDIANS

newsletter

strongheart.ouhsc.edu

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Save the date!

**National Diabetes
Prevention Meeting
Aug 21-24, 2006
in OKC**

SHS Begins Exciting New Chapter - Phase V!

Strong Heart Study (SHS) investigators were successful in securing funding for Phase V of the Strong Heart Study. New funding will allow a second examination of the Family Study participants as well as continuing follow-up of the health of the original SHS participants. Five grants were awarded by the National Heart, Lung, and Blood Institute. Grants were awarded to Dr. Barbara V. Howard, MedStar Research Institute, for the Arizona field center and central laboratory; Dr. Elisa T. Lee, University of Oklahoma Health Sciences Center, for the Oklahoma field center and the data coordinating center; Dr. Lyle G. Best, Missouri Breaks Industries Research, Inc., for the Dakotas field center; Dr.

Richard B. Devereux, Weill Medical College of Cornell University, for the Cardiology Reading Center; and Dr. Jean W. MacCluer, Southwest Foundation for Biomedical Research, for the genetics laboratory and analysis center.

The Strong Heart Study was initiated in 1988. With the new award, funding will continue the Study until 2010. With more than 120 publications to date, the SHS has contributed to better understanding of heart disease and its risk factors in American Indians and of the relationship of diabetes to heart structure and function. Based on SHS data, a prediction equation specific to American Indians has been developed to estimate

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Assessing Heart Disease Risk in Patients with Diabetes

Some studies have shown that people with diabetes are at as much risk for heart disease as people who already have heart disease but do not have diabetes. In other words, people with diabetes have the same chance of having a heart attack as people with heart disease have of having another heart attack. Because of this risk, doctors propose more aggressive treatment goals for people with diabetes.

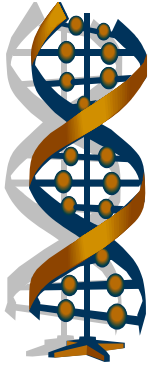
Strong Heart Study (SHS) investigators examined the influence of risk factors for heart disease, and heart disease and stroke, in 4549 SHS participants. The investigators studied participants with and without diabetes and with and without heart disease or heart disease and stroke. The risk factors for heart disease that were studied included gender, cholesterol values, albuminuria (abnormal

levels of protein in the urine), high blood pressure, current smoking, and fibrinogen (a substance in the blood needed for blood clotting).

It was found in both men and women that 1) diabetes increased the risk for heart disease and 2) heart disease risk was higher in diabetic men and women if they had unhealthy cholesterol levels

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Testing Possible Heart Disease Genes

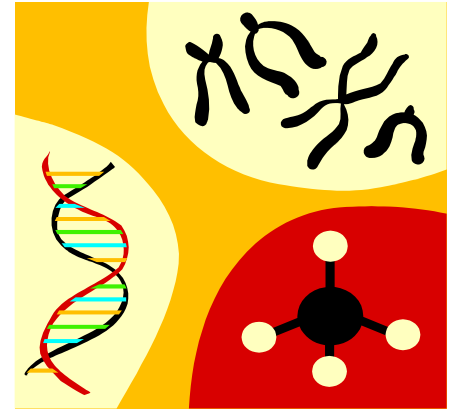


One of the main goals of SHS-Phase IV is to find out how genes we inherit from our parents affect our chances of having heart disease, diabetes, and other risk factors. This is mainly being done by a method called “linkage analysis”, which attempts to find the **location** of genes along the chromosomes, or DNA of a person. The genetic investigators of the SHS are beginning to present some of the first exciting results from this part of the study; and another article in the next newsletter will provide more details about that.

The other method of testing for genetic influences on disease is

called “candidate gene” analysis. This looks for changes in known genes that may have a possible effect on heart disease. Most of these candidate gene changes have already been suspected of increasing the risk of heart disease in other, non-Indian populations. The researcher then checks to see if these changes are present more often in people who have the condition (such as a heart attack, diabetes or stroke), compared with those who have stayed healthy.

In past newsletter articles we have described candidate gene studies that have been done in the SHS and are now reported in medical journals. The SHS steering committee has now approved two additional candi-

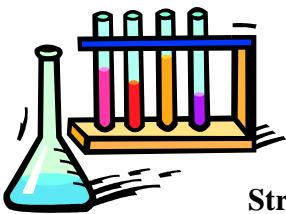


date gene studies. Research colleagues of Dr. Howard’s in Washington, DC and others will be checking on changes involving the AKT-1 gene, which seems to have a strong effect on how insulin works and on the digestion of carbohydrates. It is thought that this will tell us more about what happens in people who develop diabetes. SHS scientists working

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Recent Findings Shed Light on the Role of Fat Cells in Disease



Strong Heart Study (SHS) research helps doctors and scientists understand why some Native Americans are more likely to develop certain conditions and diseases while others are not. Even though each individual is unique within the SHS, when you look at data from large numbers of participants, some pat-

terns of disease emerge, which are known as risk factors. For example, as people get heavier, the hormone, insulin, does not work as well (known as “insulin resistance”) and the risk of diabetes increases. Similarly, having diabetes or kidney disease increases the risk of heart disease. With these risk factors clearly established, the next step is understanding exactly why overweight and diabetes are such important risk factors for heart disease.

In other words, what changes happen in the body, at a cellular level, to cause diabetes as weight goes up? What changes lead to heart disease when someone has diabetes? The Strong Heart Study plays an important part in trying to answer these questions for American Indians through continued research.

Recent work by other scientists suggests that fat cells, known as adipocytes, play an important part in

the relationship between body fatness and risk of disease. Most fat in the body is stored in fat cells. Until recently it was thought that these cells did little but act as fat stores. We now know adipose cells are active in producing a variety of protein messengers (substances made in one part of the body which tell another part of the body to do something) to change how the body works. Intriguingly, many of these protein

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Recent Findings Shed Light... *(Continued from bottom of page 2)*

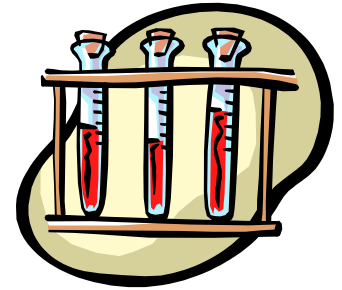
messengers also act to change levels of inflammation (response of the body when injured or “attacked” in some way) in the body. Recent studies by the SHS examined two of these protein messengers, known as adiponectin and resistin. Research on other ethnic groups suggests that these messengers relate to diabetes, overweight, and heart disease. Is this the case for American Indians?

Adiponectin is a protein made by fat cells. Oddly, the fatter a person gets the lower the level of adiponectin tends to be. We already know that lower levels of adiponectin increase the risk of getting

diabetes, but we wanted to know whether there was a relationship between adiponectin and heart disease. The SHS tested and compared stored samples from 500 participants, some of whom developed heart disease in later years and some of whom did not. We found a number of important things. We found adiponectin levels were higher in women and in persons (both men and women) without diabetes. We also found that those with higher levels of adiponectin had higher levels of HDL-cholesterol (“good” cholesterol) and higher levels of insulin sensitivity (how sensitive the cells in your body are to the effects of insulin). Levels of adiponectin tended to be lower in persons with more body fat and larger waistlines.

Adiponectin did not however predict later heart disease in our study.

Resistin is a newly found circulating protein which may affect both how the body handles glucose and the development of heart disease. Scientists at the MedStar Research Institute (Washington, DC) found raised levels of resistin in persons with atherosclerosis (the thickening of artery walls that is the basis of heart disease) in a predominantly white population. To determine if this was the case for American Indians with similar heart disease, we analyzed samples from participants in the third Strong Heart examination to assess resistin blood levels. We found that SHS participants with coronary heart disease also have higher resistin levels. Unexpectedly, however,



this appears mainly to reflect higher levels of resistin in those with diabetic kidney disease.

Studies on proteins, like adiponectin and resistin, are in their infancy. However, each year research advances, bringing with it new insights on how these and other protein messengers in the body might alter the risk of disease. It is exciting for Strong Heart investigators to be involved in such promising research that will ultimately help in designing new treatments to further cut the risk of diabetes and heart disease in American Indian communities. **SHS**



Genes...*(Continued from top of page 2)*



with others at the University of Texas in Dallas, Texas, will be testing the effects of another gene called ENPP-1, which also seems to work with insulin to play a role in the cause of diabetes. Changes in this gene have been studied in

many different populations around the world; but no one knows if American Indian people might also carry some of these changes, and what effect it might have on their health.

All of this testing is in a very early stage and whether these

findings continue to hold true after further tests, or if they ever turn out to be helpful to doctors taking care of patients, is still unknown. We are excited though, to begin the process of learning about the effect of genes on our health. **SHS**

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Strong Heart Study

Newsletter

November 2005

SAVE-THE-DATE!

August 21-24, 2006

2006 National Conference:

**Reducing Health Disparities in American Indians
and Alaska Natives by Preventing Diabetes
Throughout the Life Cycle**

*SHS investigators will make major presentations
on SHS findings*

PURPOSE

To provide a forum for sharing & exchanging information about ongoing prediabetes and diabetes prevention efforts. Focus is on community empowerment and involvement in diabetes prevention throughout the lifecycle: infancy, youth, adult, and elder.

WHO SHOULD ATTEND

American Indians & Alaska Natives interested in diabetes prevention, Special Diabetes Program for Indians grantees, tribal leaders and health program directors, health care professionals, diabetes prevention advocates and researchers, and health policy makers.

WHERE

Cox Convention Center, Oklahoma City, OK

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The Oklahoma Native American EXPORT Center of the University of Oklahoma Health Sciences Center, the Oklahoma City Area Indian Health Service (IHS), & the IHS Clinical Support Center-Accreditation Sponsor. **SHS**

SHS Phase V *(Continued from the top of page 1)*

the 10-year risk of cardiovascular disease from existing risk factors. Data have been collected that will help IHS and Tribal clinicians to better serve their American Indian communities.

There are additional benefits to the communities participating in the Strong Heart Study. Research findings have led to clinical trials to determine if interventions can be identified to reduce the risk of diabetes and cardiovascular disease in American Indians. One of these spin-off studies, the Pathways study, was conducted in the early 1990s to determine the effectiveness of a school-based intervention to prevent the development of obesity. Another spin-off study, the Stop Atherosclerosis in Native Diabetics Study (SANDS) is currently being conducted to determine if the risk of cardiovascular disease among those with diabetes can be reduced by aggressive intervention on high blood pressure and high cholesterol levels. Strong Heart investigators will continue looking for solutions as our understanding of heart disease in American Indians increases through Phase V of the Strong Heart Study. **SHS**

Assessing heart disease...

(Continued from the bottom of page 1)

and higher albuminuria, blood pressure, and fibrinogen.

Results from the SHS indicate that wide variation exists in rates of heart disease in American Indians with diabetes, depending on individual risk factors. Therefore, the investigators propose that it may be best to base treatment targets on your entire risk factor profile (which considers all of your risk factors together), rather than just the fact that you have or do not have diabetes. **SHS**