The MESA Messenger

Newsletter of the Multi-Ethnic Study of Atherosclerosis

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Success Of MESA Leads To Extension Of Study

Diane Bild, MD, MPH • MESA Project Officer
National Heart, Lung, and Blood Institute

Sometime between 2000 and 2002, you agreed to take part in the Multi-Ethnic Study of Atherosclerosis (MESA). Since then, you have been examined practically from head to toe, completed questionnaires, and had your blood drawn – most of you four times!

You have answered our phone calls and told us how you've been doing since the beginning of the study. You've also been curious about the study results - not just what we found on your exams but also what the study has found from the more than 6,800 MESA participants.

We hope that this newsletter and your MESA clinic have provided you with interesting information about MESA findings, which become more interesting and important with time, so we will do our best to keep up!

The National, Heart, Lung, and Blood Institute (NHLBI), which funds MESA, regards the study as a major success. The study has published more than 140 scientific reports, and the numbers keep growing. A few of these reports are available for your review on the MESA Participant web page (see sidebar).

Because of this success, and because of your participation, NHLBI has decided to extend the study for seven more years. While **we** are proud of this study, we hope that **you** feel proud to be part of this important project as well.

The main feature of the "renewal" will be another examination beginning in 2010. There will be more tests of the heart, arteries, and other body systems and blood tests. The staff will continue to call you from time to time... we certainly hope you will continue to respond! Your participation is more important than ever.

The MESA participant website contains lots of important information that you can use. We invite you to check back often, as we are continually adding stories of important MESA results that have been featured in the news. The *Findings* and *Links of Interest* sections have also been expanded. Please visit ***http://www.mesa-nhlbi.org/participantwebsite/***

Dr. Wendy Post to Head JHU Field Center

Dr. Moyses Szklo has stepped down as Principal Investigator of the Johns Hopkins University Field Center.

He will continue to serve as chair of the Publications and Presentations Committee and as an active MESA investigator.

The new Principal Investigator is Dr. Wendy Post. Dr. Post is a preventive cardiologist and a researcher at Johns Hopkins University School of Medicine and the Johns Hopkins University Bloomberg School of Public Health.

She is the Principal Investigator for the JHU Field Center for MESA Family and has been an active co-investigator in MESA since it began.

Dr. João Lima will continue in his role as co-Principal Investigator for the JHU Field Center.

MESA Findings

Unraveling the Connection: Kidney Function and Heart Disease

Joachim H. Ix, MD, MAS • University of California, San Diego

Previous research suggests that there may be a link between kidney function and heart disease. For instance, patients who have kidney failure are at a higher risk of developing heart disease.

This may be because the kidneys act as filters and remove wastes from our bodies; those with non-functioning kidneys have higher levels of calcium in their blood because excess amounts are not filtered out. As discussed in previous newsletters, calcium in the coronary arteries can put people at risk for developing heart disease.

Recent research suggests that subtle differences in kidney function also predict the development of heart disease over time, although researchers do not yet know why. For this study, we evaluated whether these subtle differences in kidney function in MESA participants were linked with coronary artery calcification.

We discovered that participants who had subtle kidney function abnormalities were more likely to have coronary artery calcification. However, they were also more likely to have diabetes, high blood pressure, and other cardiovascular risk factors.

With further study, it appears that coronary artery calcification is due to these other risk factors and is not a result of kidney function abnormalities. Thus, the reasons why kidney dysfunction may lead to heart disease remain unknown after this study.

However, this discovery will lead future research in other directions to determine the real connection between kidney function and heart disease.

These results were recently presented at the American Society of Nephrology national meetings and published in the **Journal of the American Society of Nephrology**.

Obesity and Heart Disease: Risky Business

Gregory L. Burke, MD • Wake Forest University

Findings in MESA continue to help expand our understanding of the effects an individual's characteristics have on heart disease.

In a paper published in the May 12th edition of the journal **Archives of Internal Medicine**, we were able to better define the impact of the current obesity epidemic in the US on heart disease risk, particularly among the different races and ethnicities studied in MESA.

This paper confirmed that excess body fat was unfavorably related to prominent risk factors for cardiovascular disease including blood pressure, blood sugar levels, and cholesterol levels irrespective of a person's age, gender, race or ethnicity.

Being overweight and obese was also related to important measures of subclinical cardiovascular disease (measured using the various high tech scans in MESA). Specifically, being obese was linked to increased carotid artery wall thickness (measured using ultrasound scans of the neck), which was a finding not previously demonstrated in other studies. Being obese was also associated with more calcium in the coronary arteries (measured from CT scans of the heart). Finally, being obese was associated with having a thicker heart wall (measured from MRI scans of the heart).

We have seen previously in MESA and other studies that these subclinical disease measures increase a person's risk for having a stroke, heart attack, or heart failure. Thus, this paper helps us better understand how an unhealthy weight can lead to cardiovascular disease.

One encouraging finding in the paper was that fewer Chinese American participants were overweight or obese. This information reminds us that obesity and resulting increase in cardiovascular disease are not necessarily inevitable. Our findings support the need to redouble efforts to increase healthy behaviors and remove barriers to maintaining a healthy weight.

Genetics and MESA: An Exciting Avenue of Research

Shannon Rhodes, PhD • Cedars-Sinai Medical Center

Several years ago, in the Spring 2004 newsletter (available at the participant website http://www.mesa-nhlbi.org/ParticipantWebsite/), we told you about a new MESA ancillary study, called the MESA Family Study.

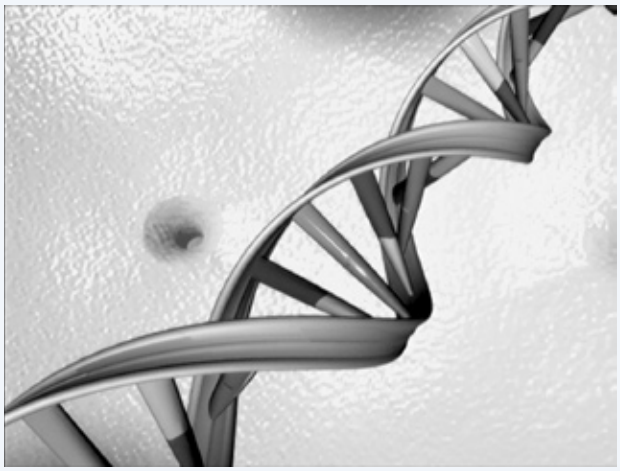
MESA was established to learn more about why some people develop heart disease and others do not. MESA Family was designed to look at this same question by looking at genes. We can look at genes because you generously provided us with a sample of your blood. From cells in your blood we can get the DNA material needed to look at genes.

During the consent process, you were given the option of allowing MESA and its affiliated researchers to use this blood for genetics studies, and we thank those willing to participate in this important research.

What are genes?

Genes contain the instructions our cells use and are encoded by our DNA. Together with the environment in which we live, genes influence many of our personal characteristics, like height, cholesterol level, and eye color.

Scientists now understand that genes may also influence which diseases people will develop. Genes are important because they provide the blueprint for proteins, which have many different important functions in our bodies. Scientists currently think that there are 30,000 to 35,000 human genes.



A Double Helix DNA Strand

Why study genes?

Many conditions such as high blood pressure, heart disease, and stroke run in families. Family members, or "blood relatives", share many factors that might influence health including their home or local environment, their lifestyles, and their genes.

So, when we see that a disease like atherosclerosis or a trait like coronary artery calcium or CAC (see the Findings from MESA section on the participant website) clusters in families, genes are one of the factors that researchers investigate.

We can study genes in families, like those of you who participated in the MESA Family Study, and we can also study genes in people who are unrelated, like most participants of MESA. The genetics studies in MESA are doing both.

Which genes are being studied in MESA and MESA Family?

Since human beings have so many genes, it is difficult to look carefully at all genes at the same time. Most genetic studies select a small group of genes (referred to as 'candidate' genes) to focus on because scientists think those genes are involved in a particular disease.

In MESA, we are currently looking at about 200 candidate genes because their proteins are thought to be important in the biological steps that lead to heart disease and atherosclerosis.

In MESA Family we are using a specially designed method to study genes in families. This method is called a 'genome scan' and is very powerful for finding new genes that might play a role in disease, namely those not currently considered 'candidates'.

These two methods, candidate genes and genome scan, are complementary because they each look for disease genes in different ways.

What can we learn from genes?

When we study genes and how they relate to a complicated disease like heart disease, we rarely get a straight answer like, "If you have the

X gene, you will have a heart attack by age 50." Sometimes, we see a strong relationship between having a specific version of a gene (known as a variant) and having a large increased chance of getting a disease, but this is unusual. More often, we find a gene variant that increases or decreases the risk of heart disease or atherosclerosis by only a small amount.

Even when a gene only has a small effect on the chance of getting heart disease, these variants can teach us about the biological processes that cause heart disease. Some genes may also make people more vulnerable to the effects of unhealthy environments or lifestyles.

This improved understanding of the causes of disease and vulnerability to disease helps us and you, because the more we know about the causes of the disease, the more targets we have for treating or slowing down the disease.

I've seen a lot of articles from MESA in the published literature. When will MESA begin publishing scientific results from the MESA Family Ancillary Study?

We are hopeful to begin publishing results from our genetic studies in the next few months. Keep watch in the MESA newsletter and on the participant web page for our scientific publications on genetics over the next 2 years.

Will I be told the results of the genetic testing?

These scientific results are different from individual genetic testing, like for the genes that influence breast cancer; we are not doing individual genetic testing and will not be providing you with any information about your own genetic makeup.

Are DNA samples in MESA used the same way they are on TV?

Many popular TV shows deal with the subject of DNA samples and DNA matching, also known as DNA fingerprinting. This is a process where the "police" laboratory tries to match two samples of DNA, one from a suspect and one from a "crime scene".

For this identity matching, the police laboratory examines regions of our DNA that are particularly unique to individuals and tries to find a match (as they do for fingerprints). Inheritance matching (paternity/maternity testing) uses this type of testing as well. In general, these regions are different from the genes that we are studying in MESA, and MESA will not conduct any DNA matching.

A Researcher Loads DNA into a Special Gel

Can these genetics studies be used to identify me?

Privacy is an important concern in genetics research. Looking at genetic information alone can identify an individual only if there is a comparison sample that is directly connected to the person's name, address, social security number, or other personal identifiers. Our laboratory will not have any comparison samples and, thus, will not be able to identify you from your DNA sample.

Protecting your privacy is one of our highest priorities in MESA. The genetic information collected for study in MESA is stored completely separate from your personal information.

There is strict oversight of the activities in the MESA study, including protecting your charts and data in locked cabinets and in password protected files, encrypting data any time it is transmitted across the Internet, and holding a Certificate of Confidentiality that allows investigators and institutions with access to research records to refuse to disclose individually identifiable research information in any federal, state or local civil, criminal, administrative, legislative or other proceeding.

The most important activity for protecting your privacy when it comes to genetic information is the use of de-identified data. We not only remove your personal information but

also "adjust" certain information like extremely low or high weight or date of birth to make sure that those values cannot be associated with any particular individual. These precautions make it highly unlikely that anyone could identify a specific person from just the genetic information collected in MESA.

There is always a small chance that, if someone has illegally, immorally, or unethically collected a sample of your genetic material and knows that it belongs to you, that person might also find a way to get access to the MESA Family genetic information and then could match the data in MESA to you specifically.

In order to make this as unlikely as possible, we are very careful about who can get access to the MESA Family data files. We train and certify all staff in protection of participants' privacy and confidentiality; we also require that all researchers have approval from a their Ethics Review Board, certification, and other controls.

How do collaborating researchers get the right to use the MESA genetic files?

Many investigators have been involved with MESA and MESA Family since the beginning, and a small number have become involved in MESA over time (like the MESA Air Pollution investigators, Winter 2006 newsletter).

To get the right to use to any of the data in MESA, these investigators have to write a proposal that includes a description of their scientific question(s), how they are going to answer the question (statistical methods), and exactly what data they would like to use. Each proposal is reviewed by a committee of MESA investigators for scientific merit (how appropriate the question and the methods are), and the proposal is either approved or declined.

At this time, Investigators from outside of MESA have to go through the same process, although their proposals are required to be much more detailed, they are required to have a MESA-affiliated investigator on their research team, and they have to commit to protecting your data as rigorously as we protect your data. Additionally, all currently ongoing MESA-related research has been approved by a Human Subjects Review Committee.

What is the future of genetic research in MESA?

In addition to looking into the approximately 200 genes and genome scan we talked about above, MESA is involved in a collaboration (partnership) with nine other research groups, all of which are interested in finding out what genes can teach us about the biology of heart, lung, and blood diseases. This collaboration, called the Candidate Gene Association Resource or CARe, is funded by NHLBI and coordinated by the Broad Institute in Boston, MA.

The genetic information produced from this collaboration will cover approximately 2,000 genes or 7% of what is currently known for humans.

Knowledge about Genetics will Lead to Better Patient Care

Again, the genetic files will be de-identified, just as in MESA itself. This de-identified genetic data is going to be made available to a larger group of research investigators who will have to go through an application process to get access to the data.

The applications will be reviewed by the National Institutes of Health (NIH), a component of the U.S. Federal Government, to assure compliance with NIH policy on protecting research participants. Other collaborations are planned and we will let you know about them as they occur.

We hope that this article has helped introduce you to the ideas and research aspects of genetics being pursued by MESA investigators and their colleagues. More information will be coming in subsequent newsletters, and, as always, investigators at your local clinical site are available to answer questions about this exciting avenue of research that has the potential to advance our understanding of heart disease and atherosclerosis.

Please Call Us If You Have Questions!

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We Couldn't Do It Without You!

The continued success of MESA depends entirely upon you and your cooperation with our efforts. Ultimately, our work together will allow doctors to provide better care to their patients and help health professionals to lessen the prevalence of dangerous diseases.

On behalf of all of the MESA staff and researchers, we **thank you** and say:
We couldn't do it without you! ♡

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