

2008

Registry Staff

- Dr. Jack Goldberg, PhD
Interim Director, VETR
- Ms. Jennifer Sporleder
Program Manager, VETR
- Ms. Esther Joneson, MA
IRB Coordinator, VETR
- Ms. Alaina Mori
Research Coordinator, VETR
- Mr. Phil Terry, MHA
Assistant Director, ERIC
- Mrs. Carrie McCloud-Gehring
Program Support, ERIC

News for Participants in the Vietnam Era Twin Registry

Consent to Continue Participation in the VET Registry

It's been more than 20 years since the Vietnam Era Twin (VET) Registry was created and in that time the VET Registry has become an invaluable national resource for cutting edge studies of health and disease. We will be asking all Registry members to provide written informed consent for their participation in the Registry. You may be wondering why after so many years we are now asking you to sign this form. Since the beginning, a top priority for the Registry was to ensure that your health information and privacy are protected. In this age of electronic record keeping we want to continue to do everything possible to protect the information you provide when you participate in a VET Registry study.

For most studies the Registry uses professional survey organizations to invite you to participate in new studies. Part of the reason we use professional survey organizations is that these companies are really good at reaching VET Registry members, even when you move or change your telephone number. Due to the mobility of the U.S. population and increasing use of mobile phones it is becoming more and more difficult to find many of our members. It's vital that we not lose track of you since we want to give you the opportunity to participate in important studies being done by VET Registry investigators.

To help locate VET Registry members we send the professional survey organization an encrypted version of your full name, last known contact information, and your Social Security number. The survey organizations use multiple means to help locate hard to find Registry members. These location methods include the U.S. post office and telephone directories. When none of these methods are successful in finding members the survey organizations turn to credit bureaus to update your address and telephone number. The credit bureaus use your name, last known address and your Social Security number to locate you. These searches at the credit bureaus are strictly limited to your address and telephone number information and *never* access your credit records. A location search like this has absolutely no effect on your credit score or record.

The VET Registry has established comprehensive data security agreements with the professional survey organizations regarding the transfer, use, storage, destruction, and re-disclosure of your information. This includes strict standards that limit the use of your information to *only* a particular VET Registry study. Your information is never sold, traded, or used for any other purpose whatsoever. After a study is completed the data are transmitted to the VET Registry and the professional survey organization destroys all your personal information.

In 2008, the VET Registry will mail you additional information about the new consent process and what is involved for you to continue your participation in the Registry. Without you the VET Registry would not exist ~ we at the Registry look forward to your continued participation.

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Published by:
Vietnam Era Twin Registry
1660 South Columbian Way
(MS: S-152-E)
Seattle, WA 98108



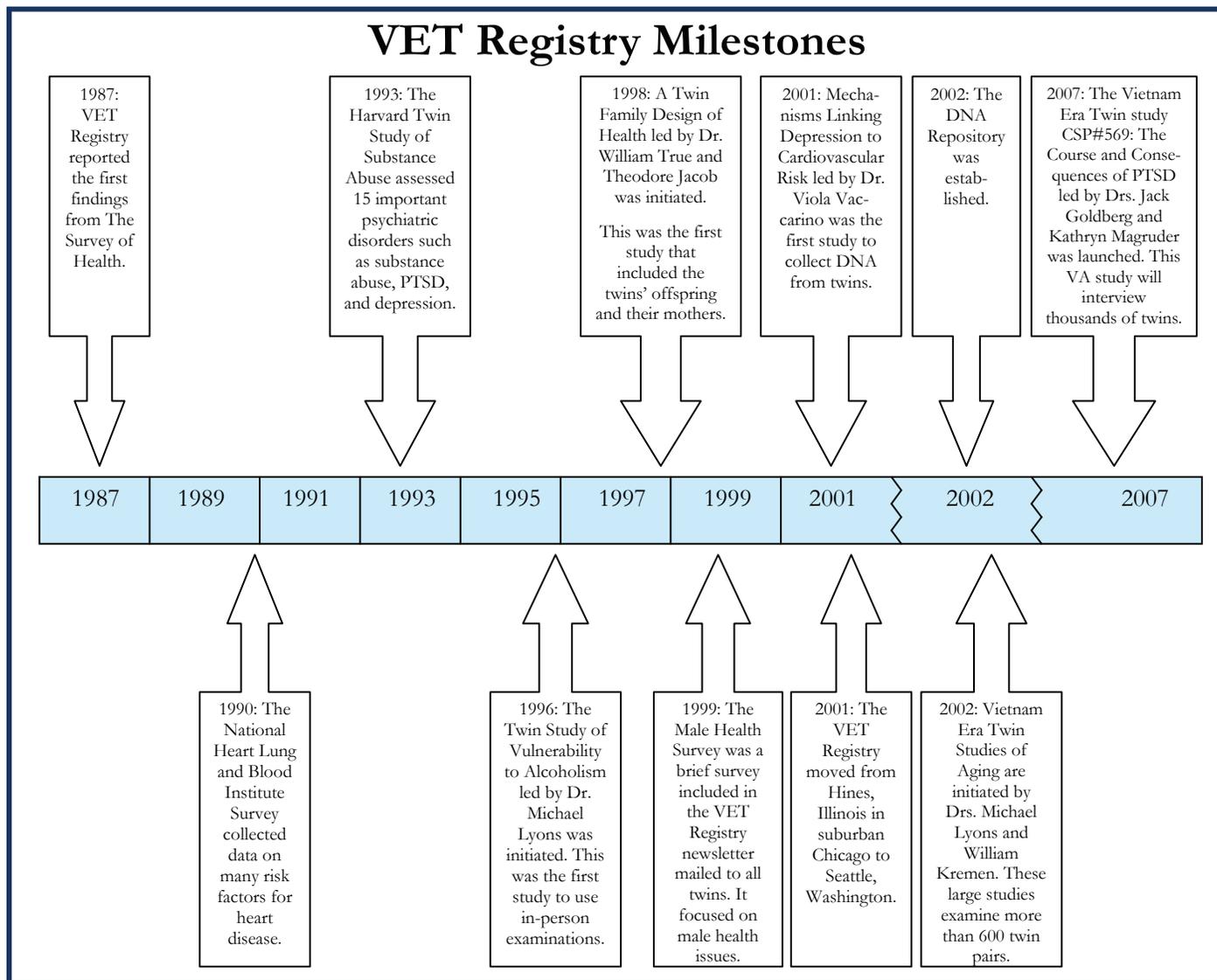
**Seattle Epidemiologic
Research and
Information Center**

About the VET Registry

Celebrating 20 Years!

Twenty years ago, in 1987, Drs. Seth Eisen, William True, Jack Goldberg, William Henderson and Dennis Robinette published the first paper describing the creation of the VET Registry. The initial goal was to determine the long-term health effects of military service during the Vietnam conflict, which was, understandably, of great concern to many veterans.

The timeline below marks some of the milestones in the history of the VET Registry.



Currently there are several important studies being conducted that are exploring health issues such as aging, memory, effects of depression on the heart, and PTSD effects on the heart. Another large study on the course and consequences of PTSD is about to get underway (see CSP Study #569 article). We are all very excited about all the scientific contributions the VET Registry has made in the past as well all the studies currently in progress. None of these studies would be possible without your participation!

We are looking forward to many more years of successful VET Registry studies.

About Research



NEW STUDY ALERT

CSP Study #569: The Course and Consequences of PTSD in Vietnam Era Veterans

An exciting new study using the VET Registry is being launched by the Department of Veterans Affairs to study the long-term course and consequences of post-traumatic stress disorder (PTSD) in Vietnam-era veterans. The study is designed to answer questions about how PTSD might influence the lives of veterans decades after the end of the war. Findings will be of interest to Viet-

“This study is designed to answer questions about how PTSD might influence the lives of veterans decades after the end of the war.”

nam-era veterans as well as veterans of more recent conflicts in Iraq and Afghani-

stan. Drs. Jack Goldberg (Interim Director, VET Registry) in Seattle, WA, and Kathryn Magruder from the Ralph H. Johnson VA Medical Center in Charleston, SC, will lead this study. This study will recruit over 9,000 VET Registry members, many of whom were previously assessed for PTSD in 1992. We will collect new data from twins using both mailed questionnaires and telephone interviews. Recruitment for this study will begin in 2008 after Registry consent is obtained.

New VET Registry Policy

The VET Registry wants to make sure you enjoy your experience as a research participant. We have always had a policy where VET Registry members were only invited to participate in one study at a time. Furthermore, we maintained a 6 month “respite period” between studies during which time we would not contact you about another study. This 6 month respite period was required whether you took part in a mail survey, a telephone interview, or a clinical examination.

We have revised the 6 month respite period to take into account the different types of research studies that involve Registry members. For example, one researcher may invite you to travel to another city for 2 days of testing while another may ask you to fill out a brief 10 minute survey mailed to your home. It is these differences that have led to our decision to alter our policy about the length of the respite period.

As of April 2008, the VET Registry will use the following guidelines for respite periods between studies:

◆ As before, VET Registry members will be invited to enroll in only one study at a time.

◆ After participation in a mail survey, telephone interview, or providing a simple DNA sample (for example, a saliva sample), there will be a minimum respite period of 1 month before an invitation to take part in another study.

◆ After participation in a clinical study, there will be a minimum respite period of 2 months before an invitation to take part in another study.

Studies will be reviewed by a VET Registry Respite Committee to make sure the guidelines are applied appropriately for each new project. The Respite Committee may decide that longer periods are needed depending on a particular study’s procedures.

If you have any comments or concerns about the respite period policy, please contact the VET Registry at 1-866-774-9647 or VETR@va.gov. We welcome your comments.

Fun Facts about Twins

Since the rise in use of fertility drugs, the rate of twin births has steadily increased. The use of fertility drugs increases the chances of fraternal birth because the drugs increase the number of eggs released. More than 75% of twin births that are a result of fertility treatment are fraternal pairs. With the more widespread use of fertility drugs some suspect that the twinning rate could become as high as 1 in 38 births in the United States.

Other factors also influence the rate of fraternal twinning. These include the age of the mother along with education and occupation. Older mothers and mothers with more education and higher income are more likely to have fraternal twins.

www.mostonline.org

<http://multiples.about.com/cs/funfacts/a/oddssoftwins.htm>

National Vital Statistics Reports - Volume 48, Number 3
- from Centers for Disease Control and Prevention

Re-Introductions

We would like to introduce and reintroduce everyone who is working on the Vietnam Era Twin Registry. There has been a recent change of directorship, with Dr. Edward Boyko leaving the VET Registry after five years as Director.

Dr. Jack Goldberg is the Interim Director. He provides overall leadership, scientific expertise and consultation with researchers from around the world. Dr. Goldberg is an epidemiologist with more than 20 years of experience in the management, conduct and analysis of complex epidemiological studies. He has intimate knowledge of the VET Registry having worked at the Registry since 1983.

Ms. Jen Sporleder assumed the role of VET Registry Program Manager in May 2005. As the program manager, Ms. Sporleder's responsibility includes the overall administration of the Registry, including data management and security and protection of the rights of human subjects. Ms. Sporleder makes sure that the day-to-day operations of the Registry run smoothly.

Ms. Esther Joneson is the VET Registry IRB Coordinator. Ms. Joneson ensures that the Registry and its studies are in compliance with all human subject protections.

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What is your Zygotosity?

Being a twin, chances are high you've been asked if you and your twin are fraternal or identical. Do you know what kind of twin you are? Many think the differences are mainly physical, but in fact the differences are much more than skin deep. Identical twins or monozygotic (one zygote) twins are the result of a single fertilized egg dividing in two. Twins who come from a single zygote share the same genetic makeup and often have similar attributes. Fraternal twins, or dizygotic (two zygote) twins, originate from two separate fertilized eggs. Because each twin starts from its own egg, genetic make-up is similar to that of other siblings born at different times; like any two siblings with the same mother and father, fraternal twins, on average, share 50% of their genetic material. Identical twins are always of the same sex while fraternal twins can be either the same sex or opposite sex.

There is also an interesting sub-group, called mirror twins. Mirror twins are monozygotic, or identical twins, but each twin has opposite features. Commonly, these features include different handedness or direction of hair curls. Only about 25% of all identical twins are mirrored. Mirror twins results from a late split in the fertilized egg.

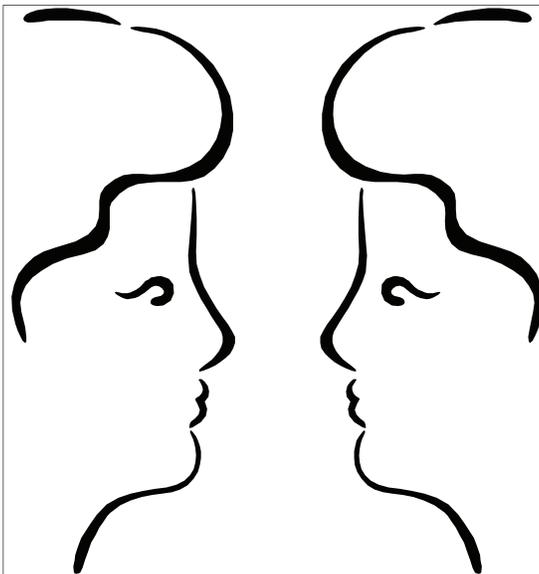
There are many ways for us to determine if you and your twin are monozygotic or dizygotic. Simply asking if you and your twin are identical or fraternal twins actually works pretty well. Years ago when the VET

Registry was first started you might recall we asked you some questions about whether you and your twin were "like two peas in a pod as children". Surprisingly this method for separating monozygotic from dizygotic twins works really well and is about 95% accurate. However, the gold standard for determining zygotosity is based on comparing the DNA between you and your twin.

Why does it matter what kind of twin you are? Most people are simply curious. But for scientists, being able to separate identical from fraternal twins is very important. Since identical twins share 100% of their genetic material any differences between the twins must be due to environment. We can understand the influence of genes and the environment by comparing how similar twins are to

one another with diseases and conditions in both identical and fraternal twins.

If you have recently participated in a VET Registry study that involved in-person testing, you and your twin may have been asked for a blood draw, a mouthwash rinse, or a cheek swab for testing zygotosity. For those twins where you both agreed to zygotosity testing we are in the process of determining your zygotosity based on DNA. In the near future, if both of you indicated you wanted to know your zygotosity results, we will mail you a brief letter with your results.



About You

Value of DNA

The Vietnam Era Twin Registry is building a DNA Repository. A DNA repository is a library of genetic material provided by twins in the VET Registry. If you participated in a VET Registry clinical study, you may have provided written consent to have a blood draw, a mouthwash rinse, or a cheek swab performed. These samples are sent to the VET Registry so that your DNA can be extracted. The value of DNA in understanding health and disease was highlighted by the completion of the Human Genome Project by the National Institutes of Health (<http://www.genome.gov/10001772>). We are approaching an era where studies on genetics and DNA are dominating biomedical research. As we learn more about genetic

“Scientists are looking towards using DNA to hopefully determine causes, cures, and ways of preventing diseases.”

influences on disease, scientists are looking to a new era of personalized medicine where DNA will be used to determine causes, cures, and ways of preventing diseases. As with all data maintained by the VET Registry we take great care with information about your genetic make-up. All the DNA samples you may have provided are kept in a locked laboratory with limited access. For each sample we assign a unique code number. No one handling your DNA in the laboratory knows anything about the sample other than the code number. The Registry takes great care to ensure that DNA information is used only for the purposes that you have agreed to.

Institutional Review Board

An Institutional Review Board (IRB) is a committee that reviews research projects, such as the VET Registry, to ensure that the safety, rights and welfare of study participants are protected. The VET Registry IRB committee is located at the University of Washington (UW) in Seattle. The committee is composed of a mix of scientists and non-scientists, affiliated and unaffiliated to the institution.

IRB committees have been around for a long time and grew out of past history of ethical and legal problems with human subject research. Recognition of the need for guidelines dealing with human subjects in research emerged following the Nuremberg trials, where the medical experimentation abuses of World War II Nazi doctors came to public attention.

Every study conducted at the VET Registry is evaluated at the UW IRB by a special committee designated for VA research. Once a study is funded, the VET Registry

submits an application to the IRB committee for review. The application includes questions about the study design, population, risks, benefits, data security, and other important information. The VET Registry must demonstrate to the IRB committee that the benefits of the study outweigh the risks.

Once a study is approved by the IRB committee, it must operate in the precise way described in the application. If there are changes to any procedure, form, or personnel working on the study, a modification form needs to be submitted explaining the changes.

In addition to the application and modifications, each year the VET Registry submits a status report to the IRB. This report serves as an update of all VET Registry activities. In this report the VET Registry must disclose any adverse events, member

~IRB continued on page 6~

Re-Introductions

~Continued from page 4~

Ms. Joneson prepares applications, renewals, and modifications to be submitted and evaluated by the Institutional Review Board.

Ms. Alaina Mori is the VET Registry Research Coordinator. Ms. Mori helps with general Registry administration and answers the Registry's toll-free phone line (1-866-774-9647).

Mr. Phil Terry is the Assistant Director for the Seattle Epidemiologic Research and Information Center (ERIC). Mr. Terry is responsible for administration of the Seattle ERIC. This includes budgeting, staffing, facilities, contract development, and liaison with the national and Seattle VA Research and Development program on behalf of the VET Registry. Mr. Terry is also involved with strategic planning for the long-term stability and growth of the Registry.

Mrs. Carrie McCloud-Gehring is the Program Support Specialist. Mrs. McCloud-Gehring's responsibilities include administrative support, making travel arrangements for VET Registry meetings, and coordinating technical support. Mrs. McCloud-Gehring is also the webmaster for the VET Registry website.

Feel free to contact the VET Registry via email at VETR@va.gov

About Twins

Did you know...

Some statistics about twins throughout the US and World:

In the US:

1 in 50 people born is a fraternal twin.

1 in 150 people born is an identical twin.

Since 1980, the twin birth rate has risen 70 percent (to 32.2 per 1,000 live births).

3.2% of all births are twins (1 in 31.25 births).

1/3 of all twins born are identical (2/3 are fraternal).

In the World:

Lowest twin birth rate is in China where 1 in every 250 births results in twins.

Highest twin birth rate is in Africa. When the mother is on a native diet 1 in 16 births results in twins.

Highest identical twin birthrate is in Japan, where 2/3 of all twins born are identical.

There are over 125 million twins in the world.

Twin Births:

About 1/3 of all twin births are male-male pairs.

Of these male-male pairs, 1/3 are identical and 2/3 are fraternal.

This means that 1/9 of all twins are identical boys and 2/9 of all twins are fraternal boys.

The most common twin combination is fraternal male-female pairs.

Recently Published Papers

1. Kremen WS, Thompson-Brenner H, Leung YM, et al. Genes, environment, and time: The Vietnam era twin study of aging (VETSA). *Twin Res Hum Genet.* Dec 2006;9(6):1009-1022.
2. Pitman RK, Gilbertson MW, Gurvits TV, et al. Clarifying the Origin of Biological Abnormalities in PTSD Through the Study of Identical Twins Discordant for Combat Exposure. *Ann N Y Acad Sci.* Jul 2006;1071:242-254.
3. McCaffery JM, Papandonatos GD, Lyons MJ, Koenen KC, Tsuang MT, Nivaura R. Educational attainment, smoking initiation and lifetime nicotine dependence among male Vietnam-era twins. *Psychol Med.* Oct 22 2007:1-11.
4. Scherrer JF, Xian H, Kapp JM, et al. Association between exposure to childhood and lifetime traumatic events and lifetime pathological gambling in a twin cohort. *J Nerv Ment Dis.* Jan 2007;195(1):72-78.
5. Xian H, Scherrer JF, Eisen SA, et al. Nicotine dependence subtypes: association with smoking history, diagnostic criteria and psychiatric disorders in 5440 regular smokers from the Vietnam Era Twin Registry. *Addict Behav.* Jan 2007;32(1):137-147.
6. Dai J, Miller AH, Bremner JD, et al. Adherence to the mediterranean diet is inversely associated with circulating interleukin-6 among middle-aged men: a twin study. *Circulation.* Jan 15 2008;117(2):169-175.

~IRB continued from page 3~

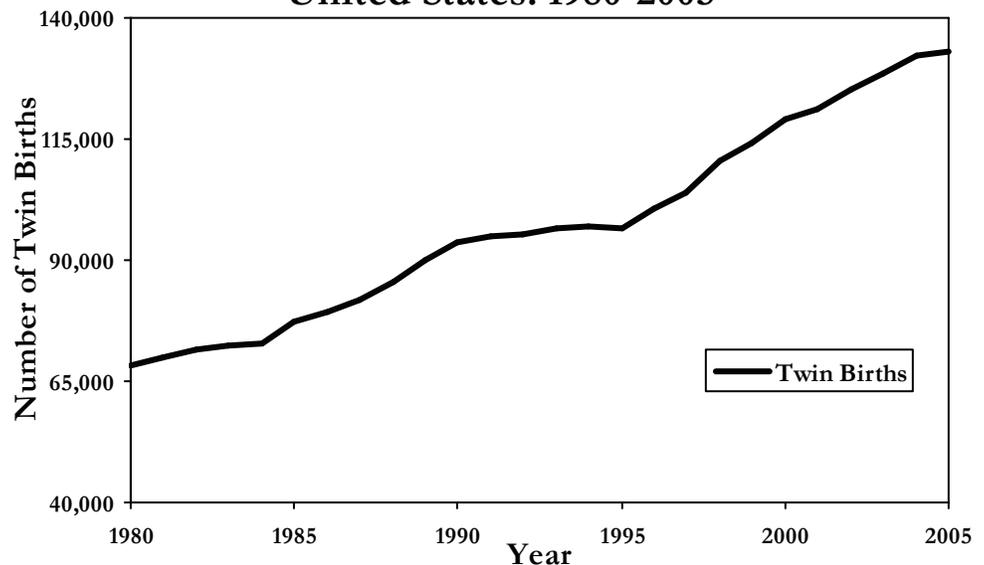
withdrawals, and any other important activities. These checks and balances help ensure that the IRB is fully aware of any study activities, and maintain the safety, rights, and welfare of study participants.

If you have any questions or concerns, we encourage you to contact us.

More information can be found about the history of the IRB at:

www.washington.edu/research/hsd

Number of Twin Births in the United States: 1980-2005



Study Summaries

Vietnam Era Twin Study of Aging (VETSA)

Principal Investigators: Drs. William Kremen, University of California, San Diego, CA and Michael Lyons, Boston University, MA.

The VETSA projects are a set of closely related studies funded by grants from the National Institute on Aging. The overall goal is learn about the different factors that make for successful aging. The plan is to follow twins over their lifespan to chart how they age. The hope is that this work provides information to help our children's generation to experience more successful aging.

Primary VETSA Project: The aim of this project to learn how genetic and environmental factors influence the aging process. We have tested over 600 VET Registry twin pairs and are studying cognition, personality and social factors, health and medical factors, and specific genes. We use a lot of complex statistics, but it's mainly about comparing similarities and differences in identical and fraternal twins. VETSA participants come to either Boston University or the University of California, San Diego.

VETSA MRI Study: Over 250 VETSA twin pairs have stayed an extra day to have a magnetic resonance image (MRI) of their brains. With these 3D images, we can measure the size and other features of the brain. We want to look at how brain functioning is determined by genes and the environment; we also want to study how the brain changes with age, and how things like memory and health are related to different parts of the brain.

VETSA Cortisol Study: Over 350 VETSA twin pairs have provided multiple saliva samples for the VETSA Cortisol Study. Cortisol, which is sometimes referred to as the stress hormone, can be measured in saliva. Cortisol lev-

els are associated with changes in stress, health, and memory. By studying cortisol, we can learn about how people's response to stress affects the aging processes.

Twin Heart Study and Vascular Disease Evaluation in Twins

Principal Investigator: Dr. Viola Vaccarino, Emory University, GA

The general objective of these projects is to investigate the influence of mental health on heart disease. The Twin Heart Study examines the effects of depression on the cardiovascular system. We enrolled 180 twin pairs, age 50-60 from the Vietnam Era Twin Registry. About half the twin pairs are discordant for a lifetime history of major depression, meaning one twin has a history of diagnosis of major depression and the other twin does not; about half the sample are identical twins and half fraternal. The main goals of this study are to determine whether certain cardiovascular illnesses are different between twins with and without depression. Data analysis for this study is now underway. The Vascular Disease Evaluation in Twins study is designed to determine if PTSD is a risk factor for cardiovascular disease. The study involves 140 twin pairs aged 50-60. Twin pairs are selected who are discordant for a lifetime history of PTSD. We will examine the effects of PTSD on cardiovascular disease and also examine how genetic and environmental factors influence the association between PTSD and cardiovascular disease. The data collection started in September 2004 and is scheduled to end in August 2008.

Family Studies of Health and Behavior

Principal Investigators: Drs. Theodore Jacob at the Palo Alto VA, CA and Kathleen Bucholz at Washington University in St. Louis, MO

Researchers at the VA in Palo Alto, California and at Washington University in St. Louis, Missouri are conducting an ambitious set of linked studies on the health and behavior of VET Registry members. This project has broadened the scope of the original VET Registry by including the offspring and wives of twins in their studies. By adding information about offspring, this lets us gain a better understanding of the intergenerational transmission of both risk and protective characteristics. Studies are focusing on behaviors like smoking and alcohol use patterns, health conditions such as obesity, and illnesses like depression. The studies involve hundreds of twins along with their offspring and wives. These exciting projects have even followed Registry members over time to see how risk and protective factors might change and how this change might be related to genetics or the environment. The twin family studies are currently on-going and involve telephone interviews with twins and family members.

Memory and Hippocampus in Vietnam Veteran Twins with PTSD

Principal Investigator: Dr. Douglas Bremner, Emory University, GA

This study examines the role that genes and the environment play in the development of PTSD. We have recruited 70 twin pairs, 60 of whom developed PTSD while his brother did not; we also have 10 twin pairs where neither twin has a history of PTSD. The study includes an in-depth clinical evaluation involving interviews, paper and pencil questionnaires, tests of memory, laboratory testing, Magnetic Resonance Imaging (MRI) and positron emission tomography (PET) imaging of the brain. Twins travel to Atlanta for these tests. The data for this study is currently being analyzed.

Name: _____

Address: _____

City: _____ State: _____ Zip: _____

Home Phone: _____

Mobile Phone: _____

Work Phone: _____

Email Address: _____



Have you moved? We would like to hear from you!

To update your contact information call 1-866-774-9647 or follow the directions below:

1. Please cut out the change of address form.
2. Fill out the form in blue or black ink.
3. Place form in an envelope, affix postage, and mail to:
 Vietnam Era Twin Registry
 1660 South Columbian Way (MS: S-152-E)
 Seattle, WA 98108

ADDRESS SERVICE REQUESTED

Vietnam Era Twin Registry
 Seattle ERIC
 1660 South Columbian Way (MS: S-152-E)
 Seattle, WA 98108