



VA BIOREPOSITORY BRAIN BANK NEWS

A YEAR IN REVIEW

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SPECIAL POINTS OF INTEREST:

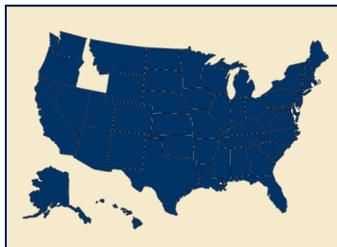
- The VABBB is now enrolling Veterans in the ALS, Gulf War, PTSD, and control brain banks
- A Navy Veteran describes his experience with ALS and his path to donation
- A VA neurologist answers FAQs
- VABBB walks to defeat ALS

Help Us Stay in Touch

- ⇒ Do you have a new phone number?
- ⇒ Are you moving?
- ⇒ Have a major health change?

PLEASE LET US KNOW!

Call toll free at
866-460-1158



Veterans in 47 states and in Puerto Rico are currently enrolled or have donated to the ALS or Gulf War brain banks.

VABBB ENROLLING HEALTHY ADULTS

In research, much can be learned from comparing brain tissue donated by persons affected by brain disorders with tissue from people who are *NOT* affected, in order to understand the causes of these conditions. Yet, most brain banks, including the VABBB, have critical shortages of tissue from those without brain disorders (otherwise known as "control tissue").

VABBB UPDATES

The VA Biorepository Brain Bank (VABBB) has had a busy year. We are currently enrolling participants for the ALS and Gulf War Brain Banks, and will be recruiting for a new PTSD brain bank starting in May (article inside). As of May 1st, the ALS Brain Bank is actively following 114 participants (111 persons with ALS and 3 Controls), and has collected tissue from a total of 151 participants. The Gulf War Brain Bank, which seeks Veterans of the 1990-1991 era, is currently following 15 participants. Gulf War Veterans may enroll in the Gulf War bank, even if they are already enrolled in the ALS bank. If you are interested in enrolling in the Gulf War Bank, please call 855-561-7827.

We are happy to report that the VABBB continues to successfully conduct tissue recoveries in 100% of cases in which we are notified by families who

want to proceed with the donation. This success is due to the dedication of the Veterans and their families in making these donations upon death, as well as the many medical professionals and others who have assisted us in performing these donations.

IMPORTANT INFORMATION FOR PARTICIPANTS:

On-Call Cell Phone Number Change

The VABBB is switching over numbers for their on-call cell phone. You should have received the new number on a **blue card**. The new number that should be used to reach us after hours is:

857-214-0992

Please update your records to reflect this new number!

HELP US SPREAD THE WORD:

You can visit the following website to learn more about the need for control tissue and tell others about our need for healthy adult participants!

http://www.research.va.gov/programs/tissue_banking/control/

VABBB NOW ENROLLING VETERANS WITH PTSD



Any Veteran with PTSD living in the United States may enroll in the PTSD Brain Bank

We are now enrolling Veterans who have PTSD and who may be interested in making an after-death tissue donation to support research.

PTSD can occur after experiencing a traumatic event. A traumatic event is something terrible and frightening that you see, hear about, or that happens to you.

Similar to the ALS study, participation involves filling out surveys by telephone, mail, or on a secure Internet website annually. These surveys will

ask for things like your name, birthdate, sex, education level, and race or ethnic group, as well as details of your military service. Some questions will ask whether you have been exposed to chemicals at home, work, or when you were in the military.

Other questions will ask about your mental health history, including whether you are currently experiencing PTSD symptoms or if you have experienced these symptoms in the past. For more information, call 800-762-6609.

Some events with the potential to trigger PTSD symptoms include:

- ◆ Combat exposure
- ◆ Child sexual or physical abuse
- ◆ Sexual or physical assault
- ◆ Terrorist attack
- ◆ Serious accidents, like a car wreck
- ◆ Natural disasters like a fire, tornado, hurricane, flood, or earthquake

VETERAN'S VIEW MAKING THE MOST OF ALS

BY: DAVID H. STAM



What Happened to Me

My Life with Books, Research Libraries, and Performing Arts

DAVID H. STAM

David Stam, a Navy veteran and historical scholar, describes how ALS has affected him, and how he came to the decision to donate to the VABBB. In the author's autobiography, pictured above, David recalls his diverse life experiences.

When I was first diagnosed with ALS in November 2008, and after I started to realize its impact, I began to think seriously about how I wanted to spend the rest of my life—however long it might be. It would have been easy to wallow in self-pity, but that I fortunately rejected. Instead, I decided to devote my time (even though there was less of it) to 1) reading or rereading great books that I had neglected, 2) trying to continue my work of historical scholarship in my field of polar history (inspired by my US Navy experience with Operation Deep Freeze, 1957-58), and 3) finding a use for my body after my death.

Thanks to the relative slowness of my form of ALS, I've been quite successful in the first two goals—I have read lots of great literature and have written and published a couple of books and several articles about my life and my Navy experiences. My Navy duty was as a journalist in the 1950s, and I travelled all over the Atlantic and Mediterranean. My most memorable voyage was to Antarctica aboard the cargo ship Wyandot, during which we resupplied one of the International Geophysical Year research stations in the Weddell Sea. On my last assignment of active duty, I was given the responsibility of managing the library of the USS Galveston while it was

IN THIS SECTION

Each newsletter, we highlight stories from caregivers in *Caregiver Corner* or from participants in *Veteran's View*. These stories describe the journey that led to our participants' decisions to donate with the VABBB.

being refurbished as a guided missile cruiser at the Philadelphia Naval base. I would spend the next forty years of my life as a librarian, completely unaware that ALS was lurking in my future. When I think back on those years, I realize how unaware I was for most of my life of the trials of handicapped

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VETERAN'S VIEW CONT. FROM PAGE 2

“After my diagnosis, I wanted to be sure that my tissue could be used specifically for research on ALS and other neurological disorders.”

people - living with ALS has been a humbling experience.

On the third objective I'm happy to report that I learned about the VA Biorepository Brain Bank (VABBB) through an article in the Muscular Dystrophy Association (MDA) Newsletter. Before my diagnosis with ALS in November 2008, I already had a living will and had decided to donate my body to the Upstate Medical Center in Syracuse for educational purposes. After my diagnosis, I wanted to be sure that my tissue could be used specifically

for research on ALS and other neurological disorders.

During the period since my diagnosis, I have seen a great deal of attention being given to football players with histories of brain damage from successive concussions, who go on to develop debilitating neurological symptoms, similar no doubt to the experience of Lou Gehrig. Some players have bequeathed their brains for research purposes and I wanted to do the same. I know that during my short naval service, I experienced some concussions (even though they

weren't often called that in the 1950s Navy). I felt the same need for the use of my own brain tissue in ALS research, and fortunately, the VABBB program has answered that wish, to my great relief and satisfaction.

HAVE A STORY TO TELL?

We would like to thank David Stam for sharing his story with us!

If you would like to contribute to the next installment of Caregiver Corner or Veteran's View, please contact us at **866-460-1158**.

NEW RESEARCH PROJECTS USING THE VABBB

The mission of the VABBB is to support ALS research in the quest for a cure and better treatments for ALS. Current projects working with VABBB tissues are summarized below.

NEW STUDIES

RNA (RiboNucleic Acid)-Based Causes of ALS

RNA plays a central role in generating proteins for a cell. Changes in cell control of RNA are considered critical in the development of ALS and other neurodegenerative diseases. Certain proteins that bind to RNA have been associated with ALS. These proteins can cause clumping of protein and RNA inside neuronal cells, contributing to the disease. The protein TDP-43 is one protein that binds to RNA and results in abnormal clumping and aggregation in ALS. The goals of this study are to determine how TDP-43 affects ALS disease and to better understand the RNA targets to which TDP-43 binds. A number of experimental approaches will be used in this research. An important and highly useful model for studies of ALS is the fruit fly (*Drosophila*), which has provided a living example for how



RNA stems from our unique DNA, and leads to the creation of proteins. Photo credit: LabGrab, by Outlier Solutions©

ALS develops over time. The flies used in this study carry a mutation of the TDP-43 protein, which will allow a better understanding of the roles of TDP-43 in ALS. Subsequent study of human ALS tissue provided by the VABBB will help support findings in the mutant TDP-43 fruit fly. This model, along with human ALS tissue, will enhance our understanding of ALS and lead to possible therapies.

microRNA in ALS

microRNAs are short (micro) RNA molecules with an important role in gene expression (the process by which the information encoded in a gene is used to direct the assembly of a protein molecule). Changes in the cell control of microRNAs have been found in ALS and other diseases. In recent years, studies have shown the potential of microRNAs for disease diagnosis. Yet, effective therapeutic use of microRNAs has yet to be demonstrated. Novel research has shown the therapeutic potential of either increasing or decreasing microRNAs in cells, depending on how the individual microRNA affects cell activity. As a first step, this study will use tissue from the VABBB to explore the types of microRNAs in the brains of ALS patients and healthy individuals. Different microRNAs found in ALS tissue will be further validated and studied for their potential use in future treatments for ALS.

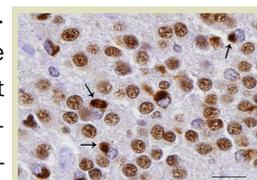


Photo showing what a buildup of proteins in the brain may look like. In this photo, the dark brown spots (marked with black arrows) show misfolded TDP-43 proteins in brain tissue. Photo credit: Feliz Geser, University of Pennsylvania School of Medicine

Ongoing Studies

The VABBB remains excited about ongoing research using VABBB tissue donated by Veterans. As presented in our previous newsletter, these studies are important for the development of treatment strategies and therapies for ALS.

Ongoing studies currently include:

- ◆ Understanding Defects in Vulnerable Brain Motor Cortex Neurons.
- ◆ Genetic Studies of Familial and Sporadic ALS.
- ◆ Promoting the Protection of Motor Neurons in ALS.
- ◆ Role of Cell-Cell Communication in ALS.

ASK A NEUROLOGIST



Dr. Manisha Thakore-James is a neurologist at the VA Boston Healthcare System and Boston University. She is also the head of the multidisciplinary ALS clinic at the Boston VA.

I've lived longer than my doctor expected I would live with ALS – Does this mean that I don't have ALS?

About twenty percent of people with ALS live five years or more, up to ten percent will survive more than ten years, and five percent will live 20 years. For example, Veterans in the VABBB have been shown to have longer average survival than the 3-5 years reported in previously published studies. For example, those Veterans who had died had an average survival (from initial ALS symptom onset) of 8 years, whereas those still alive as of 12/12/12 had an average disease duration of 14 years (1). There are many factors that influence survival with ALS - some are well characterized and other factors are still being studied.

Many factors that can influence longer survival and better quality of life can be addressed by enrolling in an ALS multidisciplinary clinic. In this type of clinic, a group of specialists will be available to address the factors that can influence an increased life expectancy with ALS. Adequate [nutrition](#) and [avoiding weight loss](#) have been tied to improved life expectancy.

Although often overlooked, [psychological and social factors](#) may play an important role in ALS outcomes. A longitudinal study has found that patients with psychological distress (feelings of stress, depression, hopelessness, and anger) have worse outcomes. It is important to talk to your doctor if you are experiencing these symptoms. Additionally, patients with incomplete forms of ALS, such as PLS or PMA, tend to have a slower progression.

References: 1) Biorepository Brain Bank: A national resource for ALS research. Christopher Brady, Katrina Trevor, Thor Stein, Eva Deykin, Sally Perkins, James Averill, Latease Guilderson, Ann Mckee, Stephen Renner, Neil Kowall. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration. Dec 2013, Vol. 14, No. 7-8: 591-597. 2) Prognostic Factors in ALS : A critical review. Amyotrophic Lateral Sclerosis. 2009; 10;310-323.

What is the difference between ALS and other motor neuron diseases such as primary lateral sclerosis (PLS) and progressive muscular atrophy (PMA)?

ALS is a disorder that typically affects two areas of the spinal cord - the corticospinal tract and the anterior horn cells. In people with ALS, only one of these areas is involved at the start of the disease. In patients with PLS, the usual muscle twitching and muscle loss seen in ALS are not evident, sometimes for several years. However, in patients with PMA, the muscle stiffness and spasms associated with ALS are not seen. ALS should be thought of as a spectrum disorder with ALS, PLS, and PMA all ALS variants. Generally, survival of patients with PLS and PMA tends to be longer.

Are there new treatments being studied?

When the "Ice Bucket Challenge" gained popularity this past summer, it led to worldwide awareness about ALS and raised more than \$100 million in new funds to support research funded by the ALS Association.

Genetics of ALS:

One new area of focus for ALS research explores the genetics of ALS. In 2011, a genetic mutation in chromosome 9 open reading frame 72 (C9orf72), was discovered. The C9orf72 mutation accounts for 10% of ALS cases and may act in a number of ways, including reducing the amount of C9orf72 protein produced, altering the protein, or causing it to interfere with cell function (see "<http://ghr.nlm.nih.gov/gene/C9orf72>" for more information). Understanding the products of this genetic mutation may provide clues as future target treatments.

Project MinE is a global collaboration with the goal to sequence the genomes of at least 15,000 people with ALS to discover new genes involved. Discovering these genes and understanding how they affect a risk for the disease can lead to new ideas for ALS treatments. See <http://www.projectmine.com/> for more information.



Photo: Researchers from the VABBB discuss projects

Environmental factors in ALS:

Although it seems that genes are important for some patients with ALS, it remains a largely sporadic disease and it is likely that environmental exposures play a greater role in developing the disease than genetics. There are some ongoing studies exploring the role of toxins in the development of ALS. Beta methylamino-l-alanine or BMAA and methyl mercury are two aquatic toxins that may have a role in the disease.

Treatments for ALS:

Another study explores use of a new delivery system for glial cell-derived neurotrophic factors using a method designed to try to overcome previous problems with getting medication to the nervous system.

Scientists have developed motor neurons from inducing pluripotent stem cells (iPs cells) from people with ALS. The development of this new technology will allow researchers to screen drugs to prevent or slow down disease progression. One area of active research is using drugs to stabilize neurofilaments in these cell lines based on work showing that ALS patients have a disruption in cytoskeletal (cell structure) proteins.

New technology:

The FDA has recently approved a diaphragm pacing system that was initially designed to help spinal cord injury patients decrease dependency on mechanical ventilation and enhance quality of life. The NewRx DPS system has now been approved for treating ALS patients in the United States.

These are exciting times for ALS research and hopefully the growth of funding spurred by Pete Frates when he started the ice bucket challenge will yield some promising treatment solutions for ALS patients.

Reference: Research ALS Today (ALS association).

Continued on Page 6

EFFECTS OF ALS ON THE MIND: A NEW RESEARCH STUDY FOR YOU AND YOUR CAREGIVER

A new study at the VABBB on cognition, behavior, and caregiver burden in ALS will be enrolling soon!

The VABBB has received funding from the Agency for Toxic Substances and Disease Registry (ATSDR) at the Centers for Disease Control and Prevention (CDC) for a new ALS study. This study will investigate whether there are risk factors for the development of cognitive and behavioral dysfunction in persons with ALS (PALS) and the effects of this dysfunction on their caregivers. We will look at



Photo Credit: Department of Veteran's Affairs

the performance of PALS on tasks that measure abilities such as attention, memory, reasoning, and aspects of mood and behavior. We will also ask caregivers to complete surveys about their mood and the challenges that they experience being a caregiver. These measures will be used to examine if there are specific patterns of changes in thinking and behavior in that may be related to greater chal-

“These measures will be used to examine if there are specific patterns of changes in thinking and behavior in [Persons with ALS]”

lenges, or burden, experienced by PALS caregivers.

In this study, we plan to in-

clude about 600 PALS and their caregivers from across the US. This is a longitudinal study, which means that we would like to re-test participants annually for this study for as long as three years. We will ask caregivers to complete questionnaires semi-annually (every 6 months). We will enroll participants in this study from two national cohorts of PALS: the ATSDR's National ALS Registry and current VABBB participants. If you are interested in participating, please contact the study staff at 857-364-2136.

VA JOINS FIGHT TO DEFEAT ALS

VA Researchers take action to help raise ALS awareness

In 2014, the ALS Ice Bucket Challenge put ALS on the map. Celebrities, Veterans, and everyday folks across the country poured buckets of ice water on their heads to raise awareness about this terrible disease. ALS is a progressive neurologic disease that has burdened the lives of thousands of people nationwide.

The VA ALS Brain Bank Team at the VA Boston Healthcare System promoted awareness by participating in the ALS Associa-

tion's Massachusetts Chapter Boston Walk to Defeat ALS® held at Carson Beach on October 25, 2014. Accompanied by family and friends, the team walked in honor of the Veterans living with ALS who are enrolled

in the VA Biorepository Brain Bank (VABBB) ALS Study. They also walked as a tribute to the deceased Veteran participants who donated their brain and spinal cord to the VABBB to support ALS research.

The VABBB team raised \$1380 through their efforts and the **ALSA Massachusetts chapter raised \$404,877.31 for research.**



Top Right and Below: The VABBB group walks to defeat ALS with ALSA Massachusetts

Left: The VABBB group ready to walk, including (from left) Sally Perkins, Latease Guilderson, Melissa Weiner, Shelley Amberg, and Christopher Brady, along with friends and family.



Does ALS ever cause personality changes or problems with thinking and/or behavior?

Changes in personality, thinking and behavior can occur throughout the lifetime of an ALS patient. The diagnosis of ALS is a life-changing event, and when this diagnosis is made, patients can go through a wide range of emotions including anger, depression, anxiety, and denial. Any response to the diagnosis by you or your family is perfectly normal and it will take time to process the information and begin to address the issues that you may face.

Some of the Symptoms that may occur include:

- Person seems to have lost “a filter” with regard to making comments or expressing opinions
 - Loss of judgment with regard to making decisions or making a decision that reflects a strong departure from views the person expressed in the past
 - Inability to concentrate or to shift focus from one activity to another
 - Behavior becomes embarrassing, inappropriate, or aggressive
- In addition, over the last decade, there has been an increase in recognition of personality changes or problems with thinking and/or behavior associated with the disease. We are learning that these changes are very important to understand and manage since they can impact the disease course, symptom management, and decision making ability throughout the illness. Genetic studies, brain imaging studies, and biomarkers are being identified to explain why these changes occur.

Reference : Living with ALS: coping and change. Marlene A. Ciechoski, MS, RN http://www.alsa.org/assets/pdfs/fyi/cognitive_changes_family.pdf

Are there any ways I can manage problems with saliva?

There are several problems that can happen with saliva management in ALS patients. If the main problem is drooling or pooling of saliva in the mouth, then medications that dry out the secretions can be very helpful. Some choices to talk to your doctor about include glycopyrrolate, amitriptyline, diphenhydramine, and hyoscyamine. Additionally, suction machines may also help you dispose of excess saliva.

The other problem that can develop is thickening of the saliva. This happens if you are breathing through your mouth. In this case, using a humidifier and drinking more fluids can be very helpful. There are also medications that can thin out the saliva. Some medications that may be used include Guaifenesin, Organidin, or Robitussin.

Other options include the use of a nebulizer that can administer inhaled medications, and the use of an apparatus called an ABI vest. This special vest is used in 10 minute intervals and can be used to help bring up secretions.

Why is tissue donation to a brain bank such as the VABBB so important?

Many of the new ideas for research in ALS stem from research on tissue donated after death by ALS patients. For example, the effects of the C9orf72 mutation mentioned above were largely supported by studies performed on postmortem patient autopsy tissue and this highlights why brain donation of ALS patients is so important for researchers. The availability of tissue from ALS patients allows researchers to understand the pathology of the disease and potential mechanisms of why the disease is happening in a way that MRIs and blood tests do not allow. Much of the progress that is highlighted in this newsletter would not have been possible without access to brain tissue from patients affected with the disease.

THANK YOU

Department of Veterans Affairs Biorepository Brain Bank



We are deeply grateful to all the Veterans who have decided to make this generous after-death organ donation supporting the VA's commitment to ALS research. While no one can say when ongoing scientific investi-

gations will discover the magical key that unlocks the secret of this destructive disease, it is certain that without the very precious gift of neurologic tissues, progress would be much slower. We are also deeply grateful to Veterans' families and caretakers who have done everything in their power to fulfill the Veterans' wishes of organ donation.

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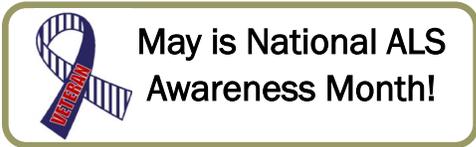
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The views expressed in this newsletter are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs



We're on the Web!
http://www.research.va.gov/programs/tissue_banking/als/