

SEATTLE Research Week 2014 TOPICS

Making A Difference

VA RESEARCH WEEK • MAY 19-23 • 2014
WWW.RESEARCH.VA.GOV

DAY 1 - DIABETES

VA Research Week is the time set aside each year to recognize the achievements of VA researchers and the generous contributions of Veterans who volunteer to participate in VA research. It is also an opportunity to call attention to the role that VA researchers play in providing high quality medical care for Veterans while advancing medical science. Each day of the 2014 Research Week we will provide information about a specific research focus ongoing at the VA Puget Sound Health Care Centers.

The VA conducts biomedical, rehabilitation, clinical, and health services research – as well as large, multi-center clinical trials – at more than 100 medical centers across the country.

The **Diabetes & Metabolism** research program at the Seattle VA Medical Center is focused in three areas. The first is beta cell dysfunction in type 2 diabetes, the most common type of diabetes among Veterans. Basic research programs have established a role for amyloid in beta cell dysfunction and are investigating endothelial (blood vessel lining) dysfunction and peptide degrading enzymes as additional contribution to the beta cell dysfunction. Beta cells are a type of pancreatic cells whose primary function is to store and release insulin. The clinical research program has identified both lifestyle and pharmacological therapies which help preserve the remaining beta cell function. The second area is the obesity that is comorbid with, and a major risk factor for, type 2 diabetes. Basic research programs have helped to identify a role for hypothalamic neuropeptides, brainstem signaling peptides, and brain reward circuits in causing the increased food intake and preference for high-sugar, high-fat foods that precede obesity. The clinical research program is investigating the role of fat in the liver, a major site of impaired insulin action. The third area is type 1 diabetes. The basic research program has identified the mechanism causing a loss of islet nerves and seeks to determine its impact on the impaired recovery from hypoglycemia that is present in this disease. The clinical research program has defined the immune markers that predict type 1 diabetes with the goal of intervening at an early stage to prevent its development.

For more information about some of the research in this area being conducted by our VA Puget Sound scientists, please visit any of these sites:

<http://www.ncbi.nlm.nih.gov/pubmed/24740208>
<http://www.ncbi.nlm.nih.gov/pubmed/24716226>
<http://www.ncbi.nlm.nih.gov/pubmed/24194506>
<http://www.ncbi.nlm.nih.gov/pubmed/24608438>
<http://www.ncbi.nlm.nih.gov/pubmed/23782941>
<http://www.ncbi.nlm.nih.gov/pubmed/23274899>
<http://www.ncbi.nlm.nih.gov/pubmed/24646311>
<http://www.ncbi.nlm.nih.gov/pubmed/24521153>
<http://www.ncbi.nlm.nih.gov/pubmed/24360972>
<http://www.ncbi.nlm.nih.gov/pubmed/23736544>
<http://www.ncbi.nlm.nih.gov/pubmed/23404441>
<http://www.ncbi.nlm.nih.gov/pubmed/23229548>
<http://www.ncbi.nlm.nih.gov/pubmed/23328128>
<http://www.ncbi.nlm.nih.gov/pubmed/23267797>
<http://www.ncbi.nlm.nih.gov/pubmed/22038516>
<http://www.ncbi.nlm.nih.gov/pubmed/24565792>
<http://www.ncbi.nlm.nih.gov/pubmed/23678881>
<http://www.ncbi.nlm.nih.gov/pubmed/23250124>
<http://www.ncbi.nlm.nih.gov/pubmed/24065622>
<http://www.ncbi.nlm.nih.gov/pubmed/23270805>

The **Prosthetic Engineering and Rehabilitation** research program at the Seattle VA Medical Center is focused on improving the quality of life and functional status of both Veterans and service members who have undergone lower extremity amputation and those at risk for lower extremity amputation and Veterans. Highlights include: 1) A large, multi-site prospective, NIH-funded clinical trial to compare outcomes of patients who receive ankle fusions (arthrodesis) and patients who receive total joint replacements (arthroplasty). Results will provide definitive evidence supporting the best clinical practice for Veteran patients; 2) Development of a VA-funded outcome model to predict mobility, wound healing, and mortality to aid Veterans and their clinicians in making difficult surgical decisions; 3) Clarifying the complex relationship between pressure and plantar location for Veterans at risk for amputation due to diabetes; and 4) and developing evidence-based recommendations for careful monitoring of patients with high pressure beneath the metatarsals.

The program's prosthetic development and design efforts have produced a field tested novel prosthesis that can expel accumulated perspiration. This novel prosthesis has resulted in greater comfort and prosthesis adherence for active lower limb amputees. It has also produced a novel prosthesis whose torsional properties can be controlled to facilitate maneuverability in less active lower limb amputees.

For more information about some of the research in this area being conducted by our VA Puget Sound scientists, please visit any of these sites:

http://www.amputation.research.va.gov/docs/Ankle_Arthrodesis_versus_Arthroplasty.pdf

<http://www.rehab.research.va.gov/jour/2013/505/page687.html>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3707817/>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3480942/>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3705894/>

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DAY 3 – HSR&D AND EPIDEMIOLOGY

Health Services & Epidemiology research program at the Seattle VA Medical Center is focused on providing complementary research expertise focused on improving understanding of the cause and treatment approaches to healthcare. The Epidemiological Research & Information Center (ERIC) seeks to improve Veterans health and health care through identifying the causes and consequences of diseases affecting Veterans. Investigators in this research groups have participated in large scale surveillance and registry studies focusing on cardiovascular disease epidemiology as well as diabetes and disease screening.

The Health Services Research & Development Center of Innovation strives to improve the well-being of Veterans suffering from complex chronic conditions. Center Investigators, often in collaboration with National and VISN partners, seek to improve patient-centered care across health and community settings as well as improve the value of care. These investigators have expertise in improving chronic disease management, coordination of care within and between primary and specialty care, healthcare access, palliative care, health economics, comparative effectiveness research, screening and research methodology.

For more information about the some of the research being done by VA Puget Sound Health Services researchers and epidemiologists, please visit the following sites:

<http://www.pugetsound.hsr.d.research.va.gov/>
<http://www.hsr.d.research.va.gov/news/feature/alcohol0414.cfm>
<http://www.research.va.gov/MVP/default.cfm>
<http://www.seattle.eric.research.va.gov/>
<http://www.hsr.d.research.va.gov/publications/default.cfm>

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DAY 4 – PTSD & TBI

The **PTSD** and **Mild Traumatic Brain Injury (mTBI)** research programs at the Seattle VA Medical Center are focused in a number of areas. The MIRECC (Mental Illness Research Center) and Mental Health Service investigators at VA Puget Sound have made important advances in the diagnosis and treatment of combat PTSD, blast concussion mTBI, and misuse of alcohol and tobacco in combat Veterans. Researchers in this field found that when the brain persistently and inappropriately responds to the alerting effects of adrenaline (“hyper-arousal”), the treatment for distressing nighttime PTSD symptoms becomes resistant. In collaboration with the Black Veterans Support Group of Puget Sound, researchers demonstrated that the inexpensive "adrenaline blocker" drug Prazosin substantially reduced or eliminated PTSD combat trauma nightmares, sleep disruption and daytime hyper-vigilance in Vietnam era Veterans. The beneficial effects of Prazosin were confirmed in active duty soldiers returned from Afghanistan and Iraq in a collaborative VA/Army clinical trial led by VA investigators embedded at Joint Base Lewis McChord. Prazosin use to treat PTSD has steadily increased across the VA, so that approximately 100,000 Veterans nationally were treated for PTSD with Prazosin in 2013. It is now a recommended drug for PTSD in the VA/DoD PTSD Treatment guidelines.

The mild Traumatic Brain Injury (mTBI) research at the Seattle VA has focused on the effects of injuries resulting from improvised explosive devices (IEDs). Mild TBI is the "signature injury" of the wars in both Afghanistan and Iraq. VA Puget Sound MIRECC and GRECC investigators, in collaboration with UW Department of Radiology neuroimaging experts, have studied the possibility of persistent, long term brain damage caused by repeated battlefield blast concussion resulting in mTBI in both Afghanistan and Iraq Veterans years after returning from combat deployments. Their studies confirmed, by using sophisticated PET and MRI brain scans, that these Veterans' complaints of headaches, forgetfulness, difficulty with anger control and other distressing behavioral symptoms attributed to their mTBIs were indeed associated with subtle, but very real, structural and functional brain abnormalities. In addition, VA Puget Sound investigators discovered a high rate of correctable pituitary gland hormone deficiencies (especially low testosterone and low growth hormone) in Veterans who had experienced battlefield mTBIs.

Related research involving new approaches to the disturbingly high rates of tobacco and alcohol use in combat PTSD have been developed by VA Puget Sound investigators. In a large VA Cooperative Study, it was demonstrated that smoking cessation embedded in the PTSD Outpatient Clinic and delivered by mental health providers produced meaningfully higher quit rates than standard smoking cessation performed in another clinic. This "embedded" approach is being disseminated across the VA system nationally.

For more information about some of the research in this area being conducted by our VA Puget Sound scientists, please visit any of these sites:

<http://www.medscape.com/viewarticle/760070>

<http://www.ncbi.nlm.nih.gov/pubmed/23846759>

<http://ajp.psychiatryonline.org/article.aspx?articleid=1712525>

<http://www.ncbi.nlm.nih.gov/pubmed/20385245>

<http://www.ncbi.nlm.nih.gov/pubmed/24102309>

<http://journal.frontiersin.org/Journal/10.3389/fneur.2012.00011/full>

http://www.pugetsound.va.gov/PUGETSOUND/features/New_Approach_to_Smoking_Cessation_Boosts_Quit_Rates_for_Veterans_with_PTSD.asp

<http://www.ncbi.nlm.nih.gov/pubmed/21139110>

<http://psycnet.apa.org/journals/abn/123/1/237/>

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DAY 5 – ALZHEIMERS

The **Alzheimer's** research programs at the Seattle VA Medical Center are focused in a number of areas. Biomarker research has identified more than 1,500 proteins in cerebrospinal fluid. Out of those proteins, 136 were uniquely associated with Alzheimer's disease, 72 were associated with Parkinson's disease, and 101 were associated with dementia with Lewy Bodies. Additional findings show that a comparison of spinal fluid tau and ptau (181) concentrations may indicate subtle nerve changes in brain regions vulnerable to Alzheimer's disease. A longitudinal assessment of spinal fluid and position emission tomography (PET) brain imaging biomarkers is needed to determine whether these changes predict cognitive impairment and the initial onset of Alzheimer's disease.

Treatment focused findings found that regularly exercising may reduce the risk for incident dementia while taking additional vitamin C and/or vitamin E supplements does not affect a person's risk for Alzheimer's disease and that the medication prazosin improved some behavioral symptoms of people with Alzheimer's disease who had agitation and aggression. Genetics focused research in this area helped to identify genetic mutations on chromosome 14, which cause early onset Alzheimer's disease as well identifying the Presenilin 2 (PSEN2) genetic mutation on chromosome 1, which causes Alzheimer's disease. It has been determined that other genes, not yet identified, may contribute to late onset Alzheimer's disease.

For more information about some of the research in this area being conducted by our VA Puget Sound scientists, please visit any of these sites:

<http://www.mirecc.va.gov/visn20/staff/peskind.asp>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3260944/>

<http://www.nia.nih.gov/alzheimers/alzheimers-disease-research-centers>