

**News Release**

**Contact: TATRC Director of Public Affairs 301-619-7927**

**National Research Effort Aimed at Major Wartime Injury Complication**



*Neural compromise from HO surrounding the femur*

Photo courtesy of MAJ Benjamin Kyle Potter

***TATRC is coordinating research efforts to address a condition that affects 63 percent of military amputees and can cause debilitating pain, additional loss of function, and long-term infections.***

While fewer service members are losing their lives in today's wars, more survivors are dealing with the aftermath of limb loss, severe burns and serious brain damage.

Despite great efforts at rehabilitation, many are challenged by debilitating pain, additional loss of function, and long-term infections, all caused by a condition that affects 63 percent of military amputees. Wounded warriors with severe brain injury and a fracture are almost guaranteed to develop this condition.

The condition is heterotopic ossification (HO), an abnormal bone growth in soft tissues. Spiky shards of bone grow uncontrollably from the site of a fracture or amputation, creating skin ulcers and causing pain as they interfere with nerves and muscles. They can even lock joints into one position as they encase them in a bony shell.

The surgery to disentangle the excess bone from healthy tissue is difficult and complex, with a greater than 25 percent occurrence of infection and wound complications. Lifelong rehabilitation may be required to keep an affected joint from stiffening again.

### **A National Strategy**

To evaluate the state of the science on HO and coordinate efforts to bring attention and resources to this problem, the U.S. Army Medical Research and Materiel Command's Telemedicine and Advanced Technology Research Center (TATRC) gathered medical researchers and clinicians in San Antonio, Texas, earlier this year.

The meeting was co-chaired by LTC Rachel Evans, research director of the Center for the Intrepid at Brooke Army Medical Center (BAMC), and MAJ Leon Nesti, a Walter Reed Army Medical Center orthopedic surgeon and a basic science researcher in HO.

While treatment and research efforts are ongoing at many medical centers to advance the care of those with combat-related injuries, the large number of orthopedic trauma patients with TBI treated at Walter Reed and the severe burn and orthopedic trauma cases treated at BAMC provide two specific populations to compare. According to TATRC director COL Karl Friedl, coordinating clinical research between these two major medical centers is an excellent opportunity to analyze and compare distinct reactions to different injury types.

Friedl said, "We need a collaborative, international effort to solve the problem of HO and improve the care of our injured warfighters. TATRC's goal is to help generate a framework that will coordinate basic research and clinical application in order to do this."

### **The Questions**

Meeting participants compiled a long list of research questions to address about HO, ranging from prevalence to causes to treatment. For instance, it appears that HO is seen more frequently in combat casualties now than in the past, but no definitive studies on this have yet been conducted.

Said Nesti, "If it is more prevalent, we need to know why. Are certain practices in the initial care management of the wounded Soldier contributing to HO? What about infectious agents? And how do brain injury and metabolic disturbances affect HO?"

All agreed that HO is somehow linked to the body's inflammatory response, and that understanding the molecular triggers could lead to a way to prevent the unwanted bone growth.

Added Evans, “At the Center for the Intrepid, we work to rehabilitate our country’s most severely injured service members. All of the clinicians here believe prevention of HO should be the primary goal of a national research effort. This will solve the problem far more effectively than simply trying to relieve symptoms.”

### **Wound Healing Gone Awry**

Promising strides have already been made in understanding HO and healing at the molecular level.

NIH researcher Dr. Wesley Jackson presented his group’s work on mesenchymal progenitor cells (MPCs). They have concluded that MPCs support tissue regeneration by suppressing inflammation and stimulating wound healing. He explained, “In blast injuries, the muscle is obliterated to the point that the MPCs may misinterpret the body’s responses to trauma. As a result, the dysregulated MPCs differentiate into osteoblasts (cells that make bones), thus creating HO.”

His group has documented different expression of genes and different growth factors in trauma versus control muscle.

CDR Eric Elster of the Naval Medical Research Center agrees that HO is related to a systemic response that is out of control. He presented his group’s work on wound healing and HO, focusing on the inflammatory response.

His group is using new Raman “optical biomarker” technology to look at the structure of tissue, visualizing peaks that can show the previously unseen differences between healing and nonhealing wounds. They have found biomarkers predictive of developing HO in combat wounds.

Elster said, “We must keep working back and forth between clinical research and lab work. We are all uncovering the same systemic response phenomena regardless of the injury type. Working together will get us closer to answers on wound healing, HO and infection—for improved care and faster return to duty.”

### **Next Steps**

Meeting participants prioritized a set of action items, including developing a common animal model. To focus research on identified gaps, TATRC is supporting an upcoming symposium with NIH’s National Institute of Arthritis and Musculoskeletal and Skin Diseases and other organizations.

Said TATRC chief scientist Dr. Charles Peterson, “It’s imperative that we discover what we can do to prevent HO and reduce the personal toll for the wounded as well as the burden on those who care for and about them.”