

# Readiness Through Research

Commander Forest R. Sheppard, U.S. Navy trauma surgeon, currently heads the Expeditionary and Trauma Medicine Department, Combat Casualty Care and Operational Medicine Directorate at the Naval Medical Research Unit San Antonio. CDR Sheppard is a principal investigator leading a dynamic team in trauma medicine research and also serves as Chair of the Navy Medical Research and Development Combat Casualty Care Working Group. He is a member of the DoD Joint Program Committee for Combat Casualty Care (JPC 6), Forward Surgical Steering Committee, and the Hemorrhage and Resuscitation Steering Committee. CDR Sheppard received his medical degree from the University Of Virginia School of Medicine and is board certified in Surgery and Surgical Critical Care. His awards include the Joint Service Commendation Medal, Navy and Marine Corps Commendation Medal (two awards), Navy and Marine Corps Achievement Medal, NATO Medal with Clasp ISAF, and over 20 combined campaign medals and service medals.



## Navy Medicine and the Evolution of Combat Casualty Care

Located on the San Antonio Military complex, the U.S. Navy Medical Research Unit San Antonio (NAMRU-SA) is one of eight subordinate research commands in the global network of laboratories operating under the Naval Medical Research Center. NAMRU-SA's role in Navy medicine research is to improve readiness and enhance future capabilities through vital work in combat casualty care and military operational research.

**Combat & Casualty Care Editor Kevin Hunter spoke recently with Commander Forest R. Sheppard**, head of the Expeditionary and Trauma Medicine Department, Combat Casualty Care and Operational Medicine Directorate at NAMRU-SA, about how the unit works to enhance the health, safety, performance, and operational readiness of Navy and Marine Corps personnel, and address their emergent medical problems in both routine and combat operations.

**C&CC: Please discuss NAMRU-SA's research and development capabilities.**

**CDR Sheppard:** At NAMRU-SA, basic and advanced development research is being conducted in the arenas of combat casualty care and operational medicine (CCC&OM) and craniofacial health and restorative medicine (CH&RM). Our core capabilities include: expeditionary trauma medicine, which encompasses hemorrhage, shock, resuscitation, and test and evaluation of field medical devices; molecular biology and immunology-based bioassay development; testing and evaluation of biomaterials; research and development of micro and nanomaterials for drug delivery and tissue engineering; epidemiology; and dental materials-related environmental surveillance. Every NAMRU-SA project is directed toward the development of life-saving or health-improving technologies that will result in better outcomes for warfighters.

**C&CC: Regarding hemorrhage control in combat, talk about your research and CCC&OM's current technology focus.**

**CDR Sheppard:** Overall, our group focuses on traumatic hemorrhagic shock and resuscitation. The evaluation of interventions

to stem hemorrhage, control hemorrhage, and provide subsequent resuscitation are quite complex and include metabolic, immunologic, and coagulation effects, not only of the original injury, hemorrhage, or shock state, but also in response to the resuscitative intervention(s). Our scientists test and evaluate hemorrhage control devices such as tourniquets, which are our first line of defense, using synthetic cadavers (SynDavers) and HapMed mannequins. NAMRU-SA's goal is to get the most effective products that are approved and available for medic use into the field or appropriate medical setting.

We also look at shock and resuscitation. Innovative research is underway to develop and test in-laboratory assays to help us understand the molecular aspects of the immune response to shock and the long-term effects of shock in warfighters. Our lab is focusing on the underlying mechanisms responsible for the observed clinical outcomes from shock, which will aid us in understanding why certain therapies work





CDR Sheppard (center) discusses the evaluation of interventions with Dr. Randy Crossland and Kassandra Ozuna in NAMRU-SA's lab in the Tri-Services Research Laboratory, San Antonio, TX. (NAMRU-SA Public Affairs)

and others do not.

A similar approach is taken with resuscitation fluids and blood replacement products. The effectiveness of the product is tested along with the effect on immune systems to determine human compatibility and appropriateness for adoption by the military. A more thorough knowledge of cellular responses and activity will permit us to refine and improve our approach to treating trauma and will, in the end, increase translatability to combat casualties with the goal of saving lives.

#### **C&CC: Is NAMRU-SA studying how to best treat post-event shock?**

**CDR Sheppard:** Yes. Platelet-derived hemostatic agents (PDHAs)—human platelets that are either lyophilized or spray dried to permit long-term storage and immediate use following reconstitution in sterile water—are being researched. This is important because platelets as currently stored have a shelf life of only five days. These new storage methods will extend that time from days to years and greatly increase the availability of platelet-directed therapy to forward deployed troops as well as expand availability within the continental U.S. within the civilian sector. From a hemostatic perspective, these agents are very

interesting. Because of their partially activated state, they are designed to actively seek outbreaks in the endothelium (where a hemorrhage would be occurring) and bind to create a “platelet plug,” which is the first step in clot formation.

Multifunctional resuscitation fluid (MRF) [is also of interest to us]. This agent encompasses all of the attributes of whole blood—oxygen carrying capacity, platelet function, and plasma. However, these products do not require the logistical considerations of, nor are they hindered by, normal blood's limited life expectancy. MRF's are free from the requirements of freezers for storage and require only sterile water for reconstitution and use. Additionally, many of these powdered plasma products provide a more consistent coagulation protein profile as compared to traditional fresh frozen plasma and offer the potential for reduced immune responses compared to traditional plasma products. Oxygen carriers would eliminate the requirement for traditionally stored red blood cells to provide oxygen carrying capacity as a part of resuscitation.

Basically, we investigate each product individually to be able to compare each to its currently available human blood component counterpart. We also study each product in combination with MRF, for comparison to whole blood resuscitation. Taken together, these effects could result in improved blood component availability for the military



Top: Lab technician Darren Fryer operating a Heska blood chemistry analyzer. (NAMRU-SA Public Affairs)



Bottom: Scientist Dr. Antonio Macko analyzing blood coagulation data. (NAMRU-SA Public Affairs)

and civilian settings and dramatically improve the care of casualties. And, frankly, revolutionize the logistical constraints that presently hinder the use of blood products.

### **C&CC: From a continuing care perspective, what is NAMRU-SA doing to maximize positive outcomes after a hemorrhage event?**

**CDR Sheppard:** The above are more specific applications; however, we really do garner information important to better elucidating the underlying mechanisms responsible for the deleterious effects of inflammatory responses to trauma and resuscitation. Currently, the two most important medical issues are trauma-induced coagulopathy—and how to correct and prevent it—and the metabolic impact of injury and shock—and how to quickly identify the start of the process and safely correct it.

Recently, we expanded our capabilities and are now fully capable of executing research that few other labs are able to do in translational research: Real-time continuous transesophageal echocardiography to determine cardiovascular responses; [and] real-time continuous EEG to determine brain function and activity during shock to fully

understand the implications of not only the injury but also the therapy. I am greatly concerned that many scientific models fail to take into consideration brain preservation, and this EEG capability will make such evaluation and assessment a routine part of every study we do.

Additionally, we have developed collaborations with the Air Force 59th Medical Group and the U.S. Army Institute of Surgical Research to leverage their focus areas in hematology, blood banking, trauma-induced coagulopathy, and ischemia-reperfusion injury, all of which feedback into our own work and improve the research we do with regard to global-body combat casualty care. Furthermore, NAMRU-SA has the distinct privilege of being located with the Brooke Army Medical Center, the only DoD Level 1 trauma center. My collaborators at the bench-top are my clinical colleagues in the trauma room and emergency department. This close working relationship facilitates the movement of medical issues from the bedside to the bench and then back to bedside. This may be the only location in the DoD with the ability to deliver pertinent, translational “bench to bedside and back” research that fills these types of military medical gaps.

### **C&CC: You often say “No one else is doing what we do.” Talk about NAMRU-SA’s unique capabilities and facilities.**

**CDR Sheppard:** We are in the unique position to have the Air Force and Army as day-to-day collaborators and “office-mates.” This, in and of itself, is unique because it mirrors the camaraderie that occurs in operational situations. By working together, the best of the three services are able to focus on improving the translatability of what we do for the warfighter.

A very distinctive capability to San Antonio is the Tri-Service Laboratory. The 181,000-square-foot facility supports a full range of combat casualty care research using small and large animal models. The facility houses a 45,000-square-foot vivarium that provides full service animal husbandry, five state-of-the-art surgical suites, seven procedure rooms, fluoroscopy and digital X-ray capabilities, and a highly trained histology/pathology team. NAMRU-SA has the best veterinary sciences team in the area, and probably across the country, ready to support any research protocol utilizing any combat casualty care model. This team supports all investigators, and it is all available under one roof.

The command is [also] fortunate to have a number of biomedical engineers to lend their expertise to the more technical aspects of our studies. The bioengineers design, build, and operate a wide range of equipment to facilitate unique experiments. In addition, we have a post-doctoral program that has recruited some of the best young researchers in the country to bring their state-of-the-art science expertise to bear on our combat casualty care projects. These hard-working researchers have brought new perspectives to some of our most challenging research questions and have become an invaluable part of our team.

Lastly, the NAMRU-SA research staff was brought together with the aim of building a multi-disciplinary approach to research. Scientists, research associates, and laboratory technicians come from varying degree fields and specific areas of study to ensure the approach to solving combat-related medical issues is well-rounded and complete. This process is unique, and it greatly benefits the researcher and research. ■

**More info:** [www.med.navy.mil/sites/nmrc/pages/namrusa.htm](http://www.med.navy.mil/sites/nmrc/pages/namrusa.htm)