

University of Nevada School of Medicine

TRAUMA INSTITUTE

Funded Population Based Studies

Our mission is to enhance the quality of life by providing leadership in intentional and unintentional injury prevention from a variety of sources including basic biomedical science, domestic violence, suicide prevention, emergency medical services for children and crash outcome data evaluation systems.

The Trauma Institute of the Department of Surgery is facilitating the expansion and upgrading of the trauma system by leading the effort to develop population based studies of injuries and their presentation. This includes Injury Prevention and Control/Epidemiological Analysis and expansion of the Crash Outcome Data Evaluation System (CODES) and Suicide Prevention and special care for target groups such as children.

The Trauma Institute has been awarded multiple continuing major grants to perform data collection on significant trauma related problems.

**CODES - Crash Outcome Data Evaluation System
October 1997 - September 2003**

CODES is a federally funded project developed by the National Highway Transportation Safety Administration (NHTSA). Only six states in phase I were funded nationally to perform data base linkage, and then analysis of automobile related injury. In Nevada alone, the cost of automobile related injury and damage was estimated to be 80 million dollars a year. The Trauma Institute was selected to lead a statewide effort to coordinate this study with leading state agencies such as the Nevada Department of Transportation, Department of Human Resources, and Emergency Medical Services. This program is funded through September 2003. It is our intention to not only continue the project beyond that date but to expand its efforts to the inclusion of crash investigators in the data collection process which will alleviate the burden of law enforcement to collect detailed crash related data and allow them to do what their mission is: law enforcement, not paper work. Clark County is the focus of this effort. A major report on this peer-reviewed grant was complete in September 2002. Continuation and institutionalization of this effort is a goal of NHTSA and the Trauma Institute.

**SUICIDE PREVENTION RESEARCH CENTER
October 1998 – September 2004**

The University of Nevada School of Medicine - Trauma Institute (UNSOM-TI), in collaboration with the State of Nevada Division of Mental Health and Developmental Services, State of Nevada EMS Division, Clark County Health District, and National Advisory Committee has created a Suicide Prevention Research Center (SPRC). The Center's goals are to conduct, evaluate and publish suicide prevention research; develop an advisory committee comprised of representatives from the eight intermountain states (NV, UT, CO, NM, AZ, WY, MT, ID); investigate suicide death investigation protocols throughout the region; provide expertise in suicide epidemiology

and prevention to other researchers, community representatives, media, students, and other interested parties; collaborate with regional and national agencies whose major focus is suicide prevention; and disseminate research findings using printed reports, oral presentations, and web-available materials.

During year five of the project the development of a comprehensive database for the purpose of base-line evaluation and ongoing surveillance began to expand from Nevada throughout the intermountain region.

On a more global basis the SPRC and its collaborators will contribute to the body of knowledge concerning suicide by designing, conducting and publishing research concerning case control studies of psychological autopsies, and differences in rural and urban reporting accuracy. Additionally we will further advance the field by the standardization of nomenclature concerning suicide including both terminology and data definitions. This study has been funded by the Center for Disease Control until September 2005.

<p style="text-align: center;">EMERGENCY MEDICAL SERVICES FOR CHILDREN March 1998 – February 2006</p>

UNSOM Trauma Institute in conjunction with the State of Nevada EMS office and the Clark County Health District has been funded to re-establish an EMSC presence in Nevada. The definition and development of an oversight/advisory infrastructure and analysis and reporting of pediatric prehospital data have accomplished this. Additional work is needed in both of these areas to further strengthen, solidify and institutionalize them. Additionally, training support of rural, frontier and wilderness prehospital care providers has been identified as a need across the state. This need will be addressed in a phased-in distance education model. Our primary focus for this funding period addresses three main objectives:

1. Solidify and institutionalize the emerging Nevada EMSC infrastructure,
2. Further refine and standardize EMS data collection in Nevada, and
3. To develop and adopt a computer-based distance learning strategies for prehospital care providers.

A Needs Assessment Survey has identified programmatic priorities that will assist in uniform data collection throughout the state.

Using the above development work, further funding has been granted from HRSA/NHTSA to implement recommendations made by the EMS community for Disaster Preparedness for Children. This study has been funded through February 2006. Our primary focus for this funding addresses four main objectives:

1. Continue to solidify and institutionalize the Nevada EMSC infrastructure,
2. Assess state guidelines, disaster plan and work to integrate pediatric components into these plans,
3. Develop a pediatric disaster training handbook,
4. Further refine EMS data collection in Nevada.

Across the nation, there is a need for education and planning around the issues of bioterrorism preparedness. In Nevada, activities are occurring to provide continuing

education to health providers, assistance to local and statewide emergency preparedness planning and assistance in developing infrastructures where none has existed before. However, within all the current activities in Nevada, none are focused specially on the needs for children on issues of bioterrorism. It is essential that the unique needs of Nevada's children are incorporated into all state disaster plans and training initiatives. The partnership of this application's main goal is to develop a triage, transport system and bring awareness within the state to meet the medical needs for children in the event of a disaster or bioterrorism attack.

<p style="text-align: center;">TRAUMA – EMERGENCY MEDICAL SERVICES SYSTEM September 2002 – September 2005</p>

The University of Nevada School of Medicine Trauma Institute with the assistance of EMSC partnership funds #MC 00084-01 has re-established an EMSC presence in Nevada. However, additional focus was needed to establish the necessary infrastructure in the Trauma-EMS System to improve access to and quality of service for those who are severely injured. Current goals and objectives of this project reflect our aim in four areas:

1. To designate an individual responsible for the State Trauma Systems program development and facilitation.
2. Identify and convene a Statewide Stakeholder's Group of trauma-EMS participants to effectively plan, communicate and implement future State initiative.
3. To develop a statewide plan for Trauma-EMS Systems based on the findings of the State Trauma Care Systems/Disaster Readiness Survey.
4. To integrate the trauma care system plan into the overall EMS system using the current resources available to achieve statewide improvements.

These funded projects are public health projects. No fundamental research is included. Consequently, the only support for our major focus on trauma research is from Atlantic Philanthropies which in summarized below.

<p style="text-align: center;">CELLULAR RESPONSE TO INJURY January 1997 - Present</p>

Injury is the nation's leading public health problem. Its scope and nature demand greater attention so that its vast personal, societal and physical consequences can be minimized and mitigated. The National Academy of Science has called accidental death and disability the neglected epidemic of modern society. The epidemic proportions are staggering. Injury is the leading cause of death for those under the age of 45 and the third leading cause of death overall in the United States. It strikes the young disproportionately, causing 80% of teenage deaths and 60% of childhood deaths; the peak death rate comes in the 25-44-year age group.

Unintentional injury is the number one killer of children ages 14 and under. Each year, nearly 6,700 children are killed and more than 50,000 are permanently disabled by preventable injuries. Trauma causes greater loss of working years of life than all forms of cancer and heart disease combined.

Specific research proposals:

1. Our studies have demonstrated a striking need for adequate volumes of saline solutions in addition to whole blood in order to prevent renal failure. Recently, the timing, volume, and rate of administration of saline solutions have been debated. Further precise delineation of these parameters needs further study. Our paper which appeared in the World Journal of Surgery will help to clarify this issue, but more studies are necessary.
2. Deaths among trauma patients who survive the first few days are most often due to infection and organ failure with the lung being the most commonly affected organ. Having an ongoing research laboratory allowed us to translate basic research into clinically relevant facts. Early works by us and others on white blood cells response to injury or the subsequent infection producing cytokines (cell killers) has led to over 2000 research papers per year being done in an attempt to characterize and modify these bodily responses to injury.

The need for restoration of fluids in addition to blood appears to consist primarily of sodium containing fluids. Lactated Ringer solution and normal saline have been used most frequently with outstanding results beginning with our studies and patients treated during and since the Vietnam Conflict. However, with severe shock, some patients have shown alterations in host immunity. Immune effector cells such as polymorpho nuclear neutrophils are being studied with different sodium containing fluids. Also being evaluated are the programmed cell death (apoptosis) response to different fluids, with a new method of measurement.

3. Research is still needed to (a) identify the determinants of irreversible cellular damage and (b) develop means of modulating cellular/subcellular response to injury, so that surgical and other interventions may be optimized to prevent mortality or minimize morbidity. Sepsis (the invasion of host tissues by microorganisms, with the resultant presence in the blood of microorganisms, toxins, and/or inflammatory cytokines) is the leading cause of late death, preventable morbidity, and excessive cost in the treatment of trauma patients.

Progress during the past year has been extremely satisfying. The effects of the cytokines, which are released by tissues including white blood cells has been impressive. It has been demonstrated that shock from infection is dramatically influenced by the excessive release of cytokines. Furthermore, using blocking agents such as matrix metalloprotenase inhibitors and other inhibitors which blocks the production of cytokines has shown a remarkable ameliorating effect on the response to injury.

4. The effects of nutritional intervention with hydroxy- β -methylbutyrate and arginine and glutamine on body weight, body composition, muscle cross-sectional area and immune status have been evaluated by Fuller, et.al. in wasting diseases including the cachexia of cancer. These studies showed that nutritional intervention with HMB/arginine/glutamine resulted in an increase of body weight, lean body mass, and immune status in wasting diseases. This same approach should be tried following trauma. We have shown previously that the muscle wasting that occurs following trauma is not adequately reversed by total parenteral nutrition. Clinical

studies are ongoing to evaluate protein metabolism in response to nutritional intervention following trauma.

5. Obviously the ideal replacement and resuscitation fluid for various forms of shock and trauma has not yet been devised. The increasing risks associated with transfusions, as well as, periodic shortages of blood products have fueled the search for an efficacious artificial blood substitute. During the past years our laboratory has been able to make phospholipid liposome carriers. An alternate strategy to the use of lipids as carrier components is formation of polymer microspheres, using possibly compatible polymers such as polylactic acid or alginate. This approach is slow and labor intensive and has been disappointing. However, the usefulness of safe “artificial” blood is so profound it seems worth pursuing. The ideal replacement solution might consist of a saline solution containing microspheres with encapsulated antioxidants, oxygen carrying blood substitutes and/or soluble receptors, as well as, cytokine antagonists such as IL-1ra or matrix metalloproteinase inhibitors of cytokine production.