

## US DEPARTMENT OF DEFENSE BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

## Injury Models Prolonged Hypobaria During Aeromedical Evacuation and the Effects on TBI

In response to concerns by USAF Critical Care Air Transport Team that prolonged flights during aeromedical evacuation of neurotrauma patients might worsen neurologic outcomes, the USAF sponsored research to investigate the effects of exposing rats to hypobaria at different times after mild or moderate TBI. Following either impact-induced moderate TBI or blast-induced mTBI, histologic and neurologic markers of injury were worsened by six hours hypobaria (=8000 feet altitude), initiated at six, 24, or 72 hours, after injury and six to seven days after injury. Brain injury was also worse when rats were exposed to 100 percent oxygen compared to 21 to 28 percent oxygen during hypobaria. Exposure to two flights at 24 hours and 72 hours caused more damage than one flight at either of these times following impact TBI but not blast-TBI. Following impact TBI, administration of CR8, an anti-inflammatory cell cyclin-dependent kinase inhibitor, improved behavioral and histologic outcomes. TBI and subsequent hypobaria were accompanied by elevated levels of serum microparticles, which could contribute to systemic inflammation. Changes in gene expression in the brain following blast TBI and hypobaria suggest that drugs that trigger an increase in the expression of cytoprotective genes could be used to improve outcomes in these paradigms. These results support the hypothesis that exposure to aeromedical evacuation-relevant hypobaria within a few days after TBI can be dangerous. They also suggest that levels of inspired oxygen during aeromedical evacuation should not be greater than those necessary to maintain systemic normoxia. Although this study uses a rat model, it underscores the need for more work to be done to understand the human response to air evacuation. However it is important to note that the given the "perfect" time to transport a patient with a brain injury, there are many times when the operational environment and/or other injuries require rapid transport in any available platform.