Breathing the Battle: Developing a Pre-Clinical Model to Assess Military Respiratory Hazards

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Background

Millions of Gulf War era and post-9/11 U.S. Veterans were exposed to airborne hazardous particulate matter (PM) including desert dust, diesel fumes, and open-air burn pits used for waste disposal. A broad range of military, medical, and industrial waste were incinerated with jet or diesel fuel. Exposures are linked to various pulmonary diseases known as "Deployment Related Respiratory Disease" (DRRD), characterized a broad range of potential syndromes and conditions such as idiopathic pulmonary fibrosis and constrictive bronchiolitis. Clinical studies presents conflicting findings on the extent of physiological effects. Preclinical models can serve as foundational steps in providing critical insights for targeted interventions to mitigate military airborne toxin related conditions. Current literature underscores the need for comprehensive, translational research to integrate findings into healthcare practices.

Conceptual Model

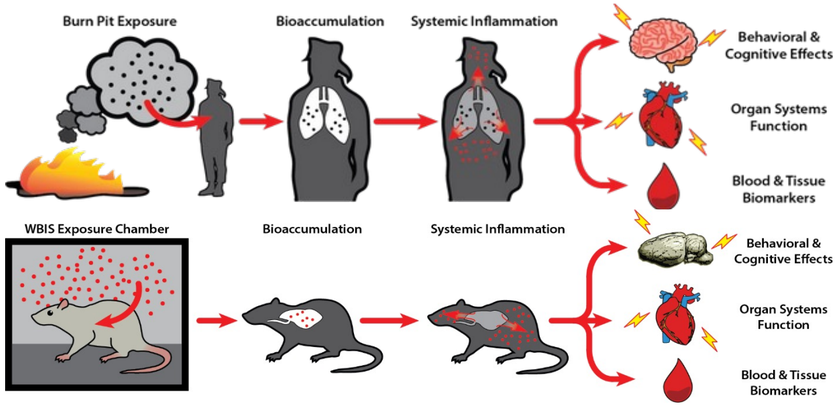

Figure 1: Advancing translational burn pit exposure research lies in effectively simulating inhalation exposures to varied mixtures. An ideal model would incorporate the incomplete combustion of input materials and deliver emissions in real-time. Many models lack the full spectrum of materials from open air burn pits, limiting their full applicability in predicting human health outcomes. Pilot studies conducted at the Center of Inhalation Toxicology (iTOX) at WVU have constructed a burn pit generator capable of burning and smoldering standardized waste using jet fuel. The emissions from the burn pits are subsequently administered to freely moving rodents within an inhalation chamber. With future studies incorporating complex mixtures, this model can serve as reliable surrogate for investigating the pathology of burn pit related health issues.

Inflammatory Biomarker Signature in Multiple Tissues

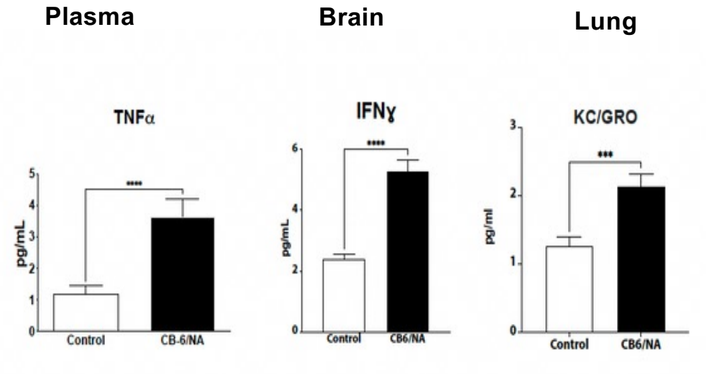

Figure 2: A common finding across multiple models is the elevation of inflammatory markers, suggesting a consistent immune response to the simulated burn pit exposures. Data highlighted by Trembley, et al 2022 demonstrates increase of pro-inflammatory markers across multiple tissue. Rat inflammatory markers measured by Meso Scale Discovery (MSD, Rockville, MD, USA) V-PLEX Rat Pro-inflammatory Panel 2 Kit (K15059Gi). Statistical analysis, unpaired t-test or Mann–Whitney tests according to data distribution (n≥8 for all biomarkers per experimental group). Control (white bars) vs CB6 (black bars). Data are represented as means ± SEM. Significance is denoted as: * $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$, ****$p < 0.0001$.

Significance to Veteran Health

Ongoing challenges in diagnosing and monitoring respiratory symptoms in Veterans after deployment, highlight the need for sensitive, non-invasive clinical assessments. It's likely that a variety of approaches will be necessary to fully understand the different pathobiologies that result from exposures. We stress the importance of robust models to explore the complex effects of burn pit exposures on health.

References

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