



# AEROMEDICAL EVACUATION-RELEVANT HYPOBARIA WORSENS NEUROLOGIC OUTCOME AND MORTALITY FOLLOWING TRAUMATIC BRAIN INJURY OR POLYTRAUMA IN RATS

**Catriona Miller, PhD, Gary Fiskum, PhD -  
University of Maryland School of Medicine**

**U.S. Air Force C-STARS Baltimore**

---

**U.S. Air Force School of Aerospace Medicine**

# DISCLOSURE INFORMATION

**I have no relevant financial relationships to disclose**

**The views expressed here are my own and not that of the US government.**

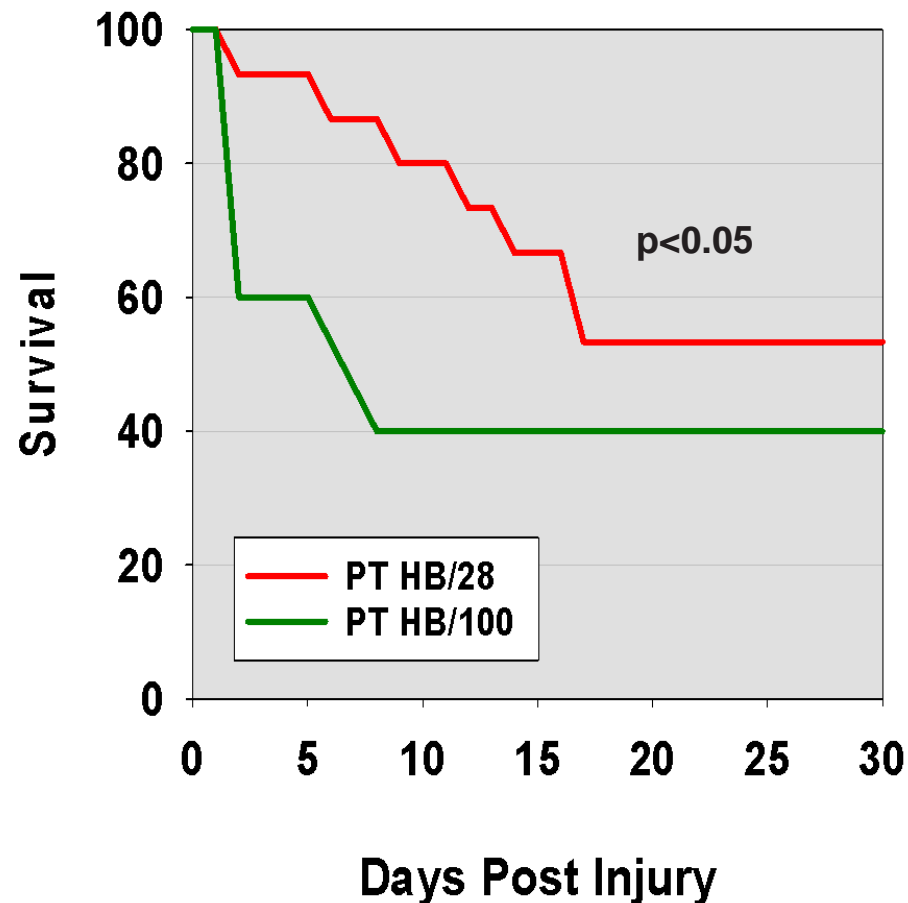
# COMBAT-RELATED INJURIES AND AEROMEDICAL EVACUATION

- Warfighters who are seriously injured are often air evacuated (AE) to a regional military medical center within a few days after injury aboard aircraft that are pressurized to the equivalent of 8000 ft altitude.
- Animal studies indicate that exposure to AE-relevant hypobaria within 3 days after isolated impact- or blast-induced TBI worsens neurologic and histologic outcomes. *(Goodman et al (2011), Skovira et al (2016), Proctor et al (2017), Scultetus et al 2016)*
- *Butler et al (2016)* found that complications among AE patients were significantly reduced when transported under a cabin pressure of approximately 5000 ft compared to 8000 ft.
- Polytrauma victims may be more sensitive to adverse effects of hypobaria. ***We hypothesized that exposure of rats to AE-relevant hypobaria after polytrauma worsens mortality and/or neurologic outcome.***

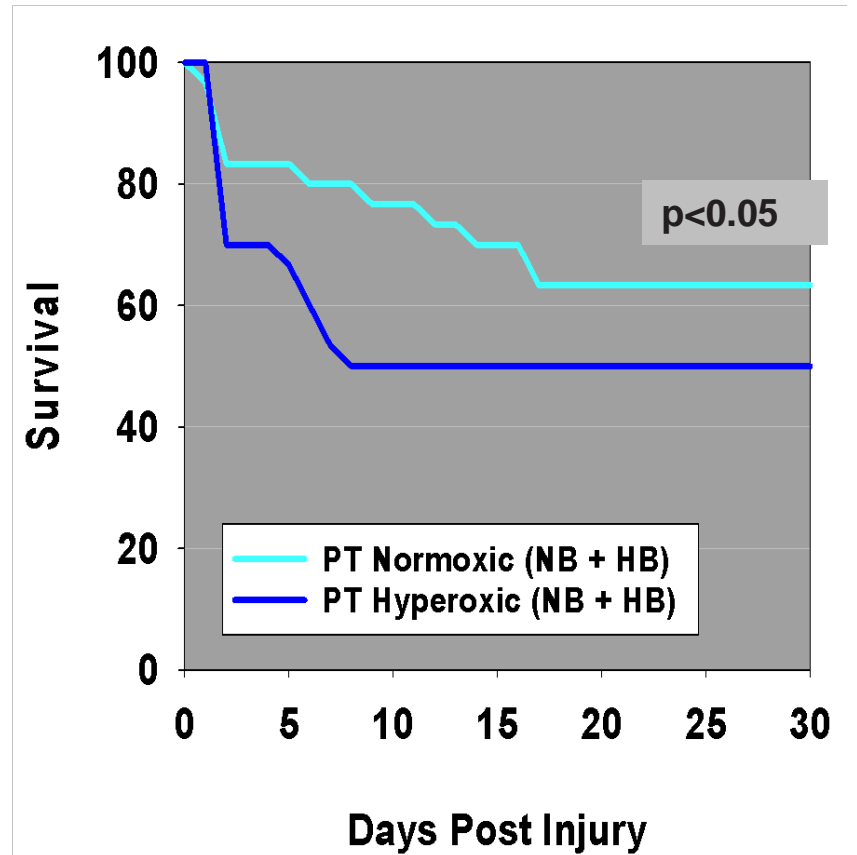
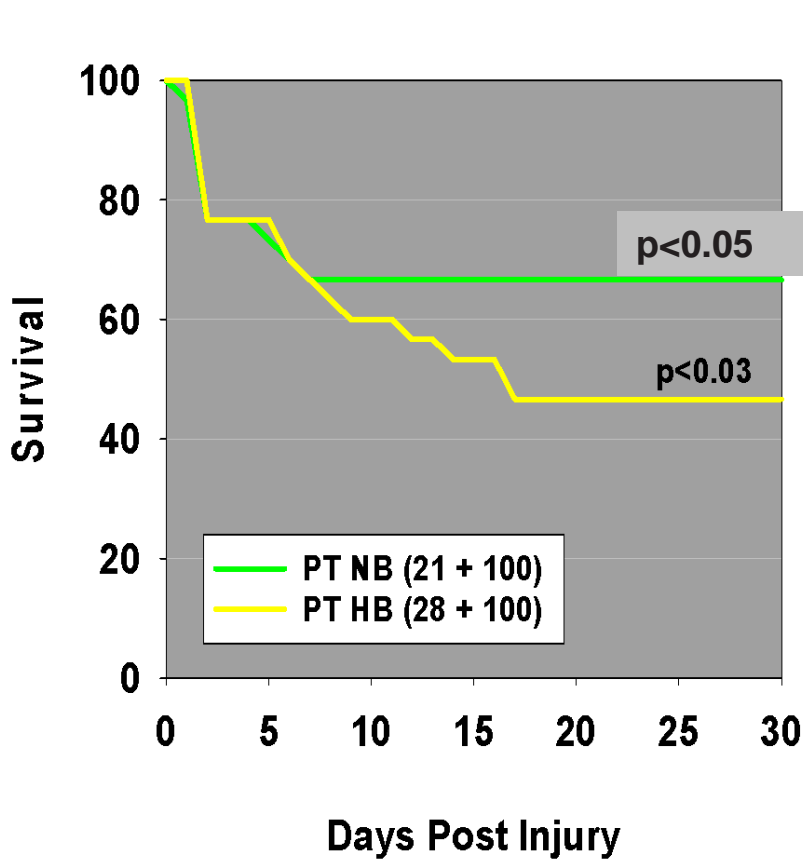
# RAT POLYTRAUMA MODEL

- Controlled cortical impact (CCI) followed immediately by hemorrhagic shock (HS) (MAP 35-40 mmHg) for 30 min. n=15 rats/group
- 1 hour pre-hospital resuscitation with Hextend
- 1 hour in-hospital resuscitation with re-infused blood
- Exposure to 8000 ft hypobarica at 24 hours under either 28% or 100% oxygen
- Exposure to sea level (in chamber) at 24 hours under either 21% or 100% oxygen
- Survival for up to 30 days
- **No mortality after CCI or HS alone +/- exposure to hypobarica but significant mortality following polytrauma.**

***Exposure to hypobarica (HB) under hyperoxia increases mortality compared to normobarica under room air.***



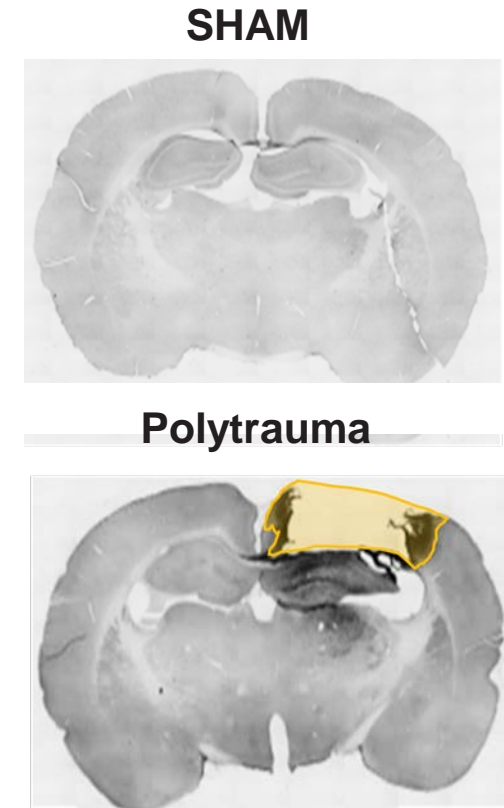
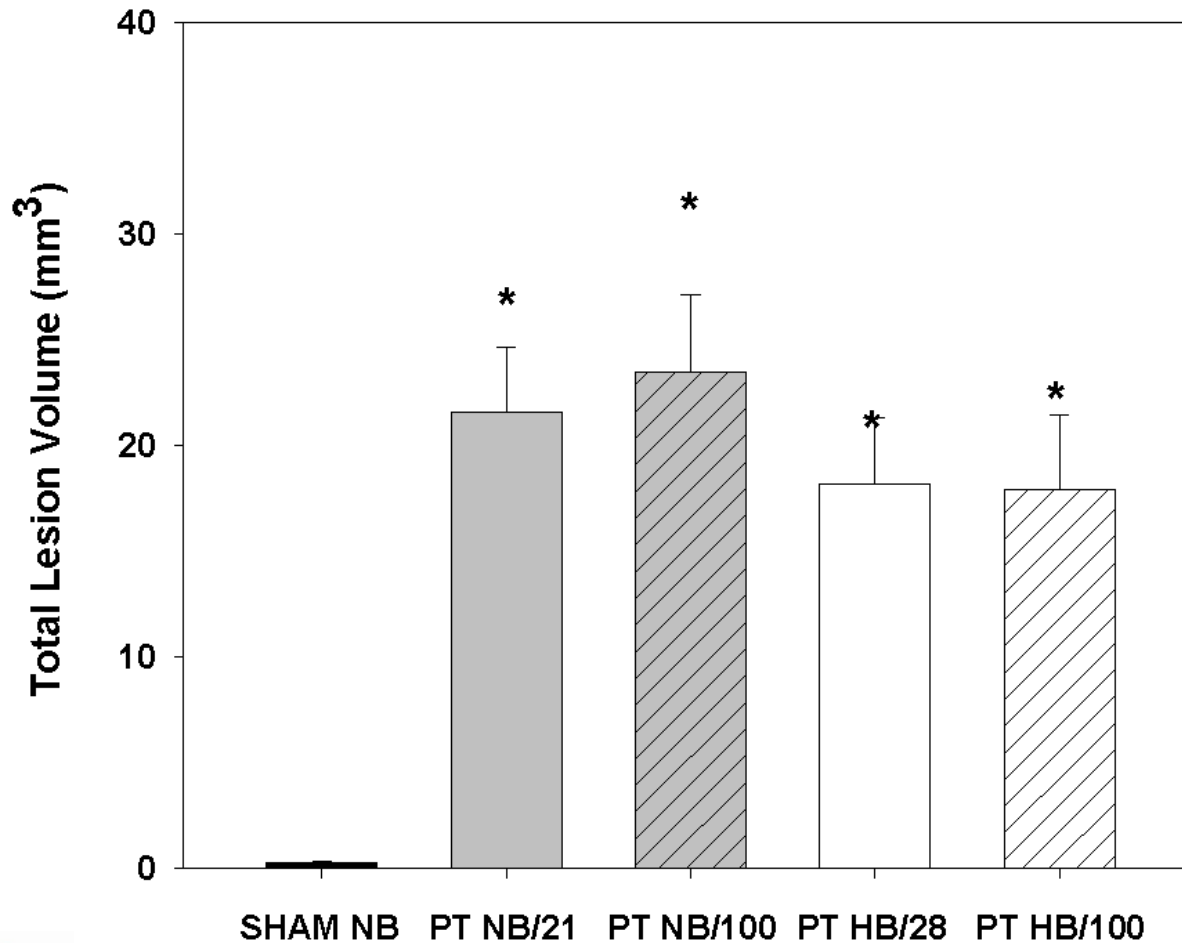
# HYPOBARIA OR HYPEROXIA INCREASE MORTALITY AFTER POLYTRAUMA



# MORTALITY ETIOLOGY

- **Worsening of brain injury**
- **Lung injury**
- Kidney damage
- **Gut injury**
- All above (**multiple organ dysfunction syndrome**)

# AFRL CORTICAL LESION VOLUME 30 DAYS POST-POLYTRAUMA



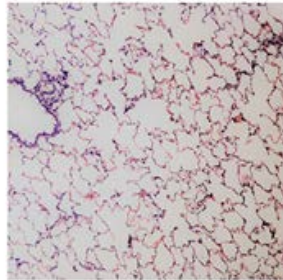
***Hypobaria or hyperoxia had no effect on cortical lesion volume for rats that survived to 30 days.***





# LUNG INJURY AT 48 HR POST-POLYTRAUMA

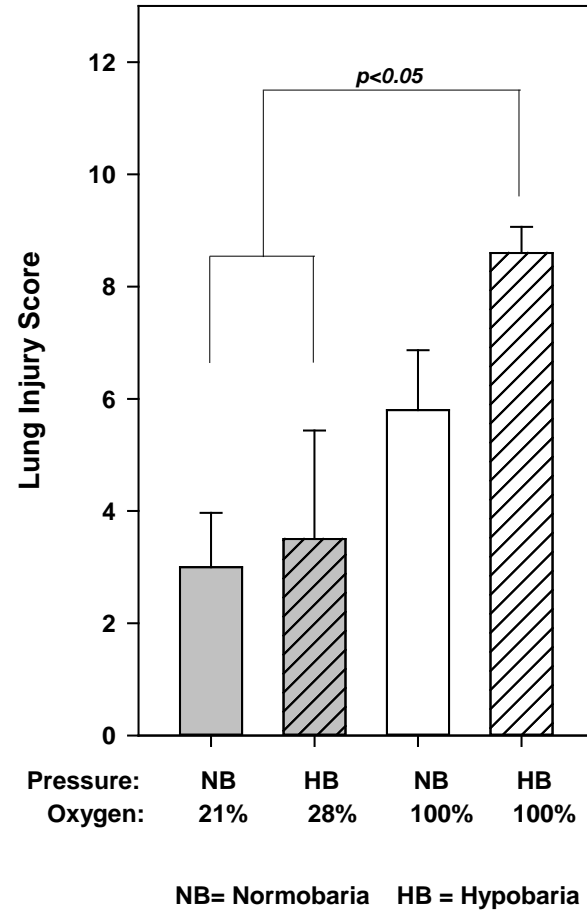
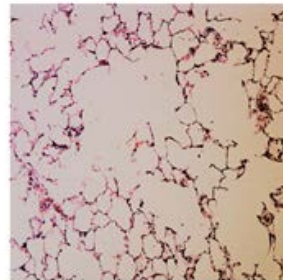
Sham



Normobaric  
21% O<sub>2</sub>

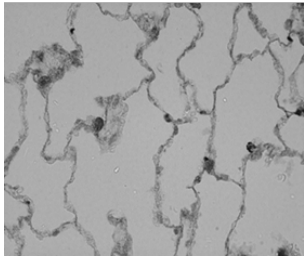


Hypobaric  
100% O<sub>2</sub>

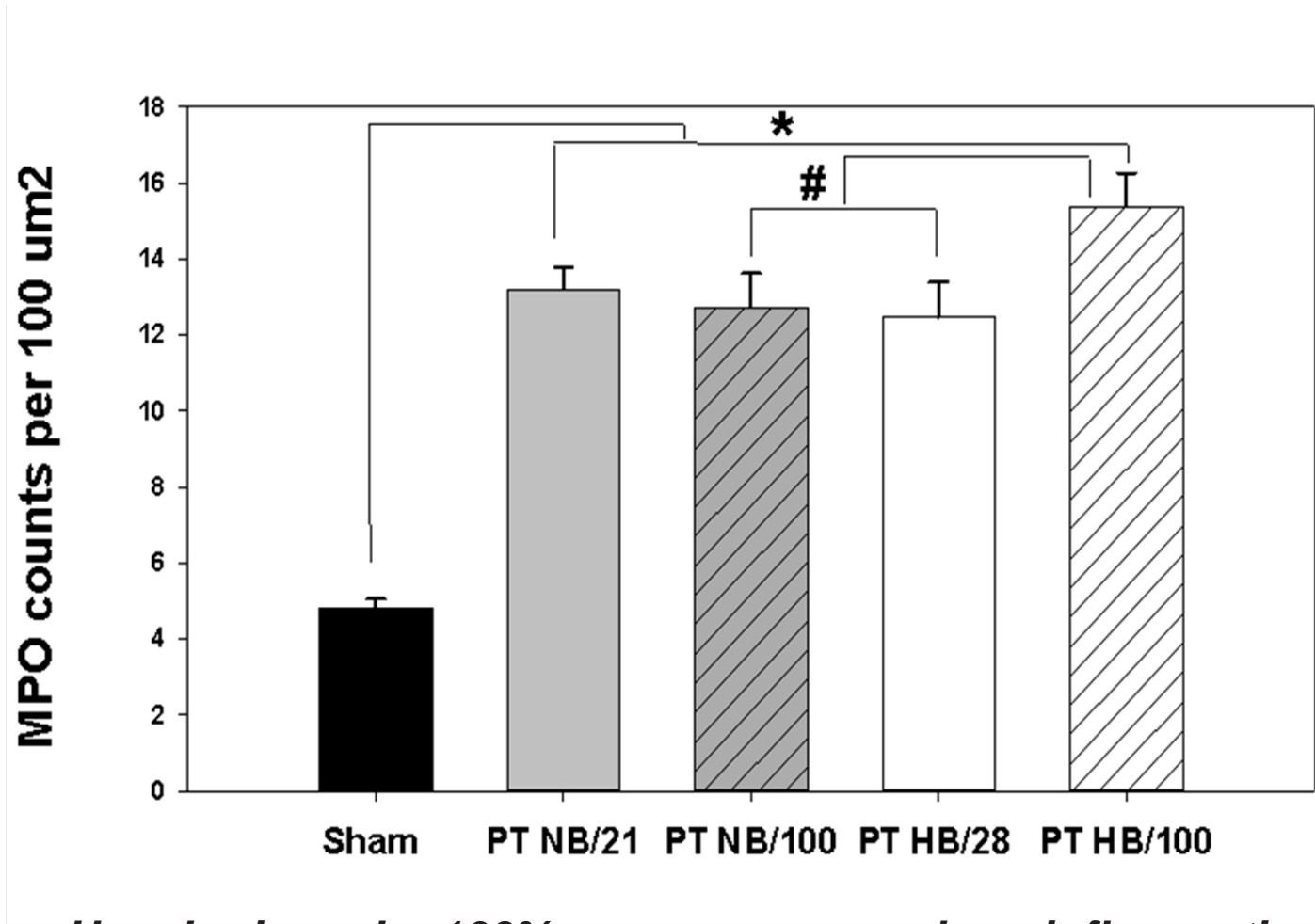
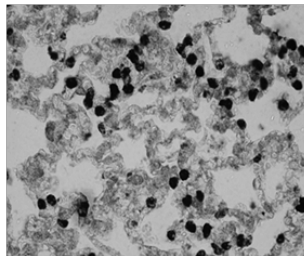


# MYELOPEROXIDASE-POSITIVE NEUTROPHILS IN LUNGS AT 48 HR POST-POLYTRAUMA

Sham



HB/100

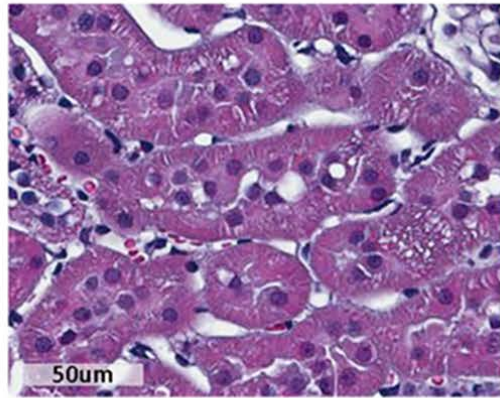


*Hypobaria under 100% oxygen worsens lung inflammation*

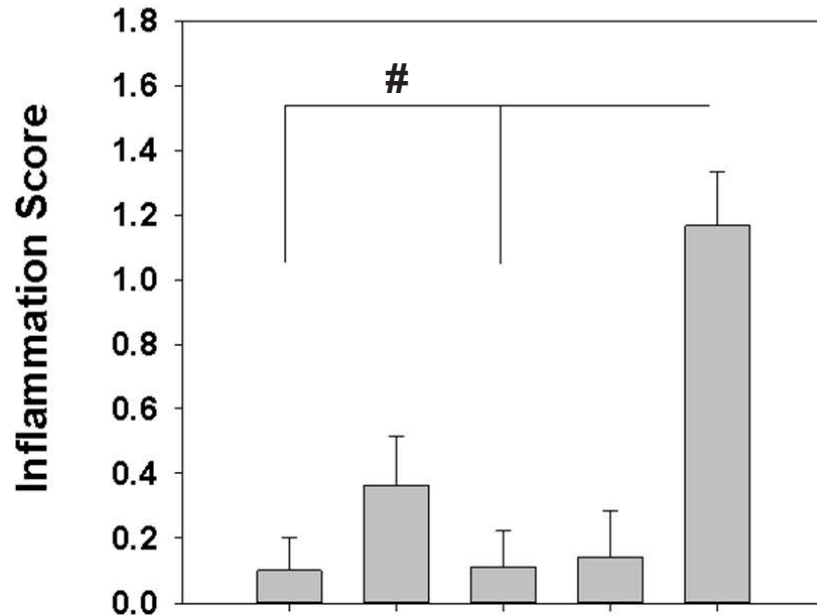
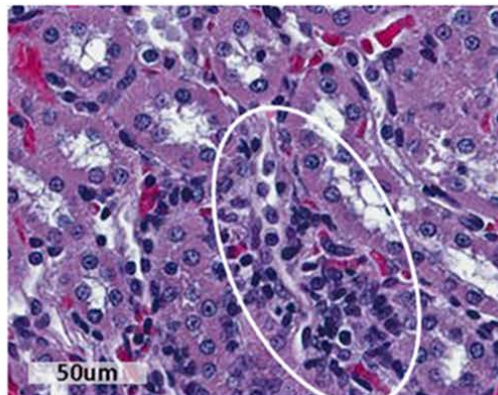


# KIDNEY INFLAMMATION AT 30 DAYS POST-POLYTRAUMA

Sham



HB/100



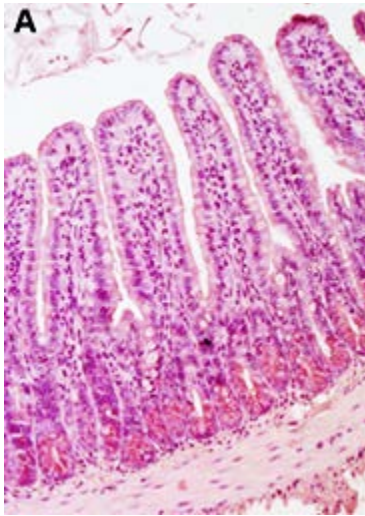
Injury:	SHAM	PT	PT	PT	PT
Pressure:	NB	NB	NB	HB	HB
% Oxygen:	21	21	100	28	100
n:	10	11	9	7	6



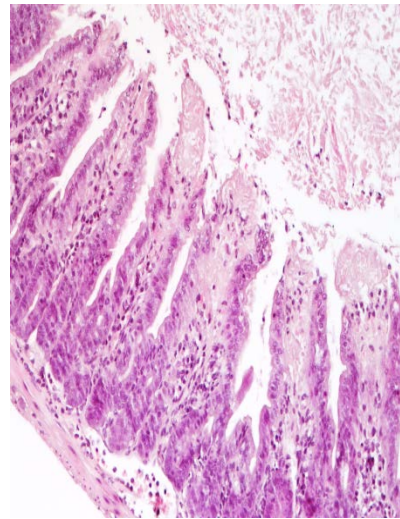
# GUT INJURY 30 hr POST-INJURY



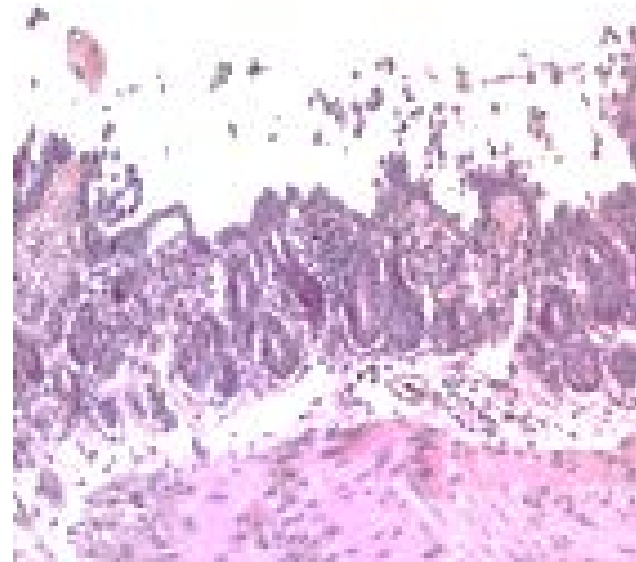
*Every Airman a Force Multiplier*



**Sham**

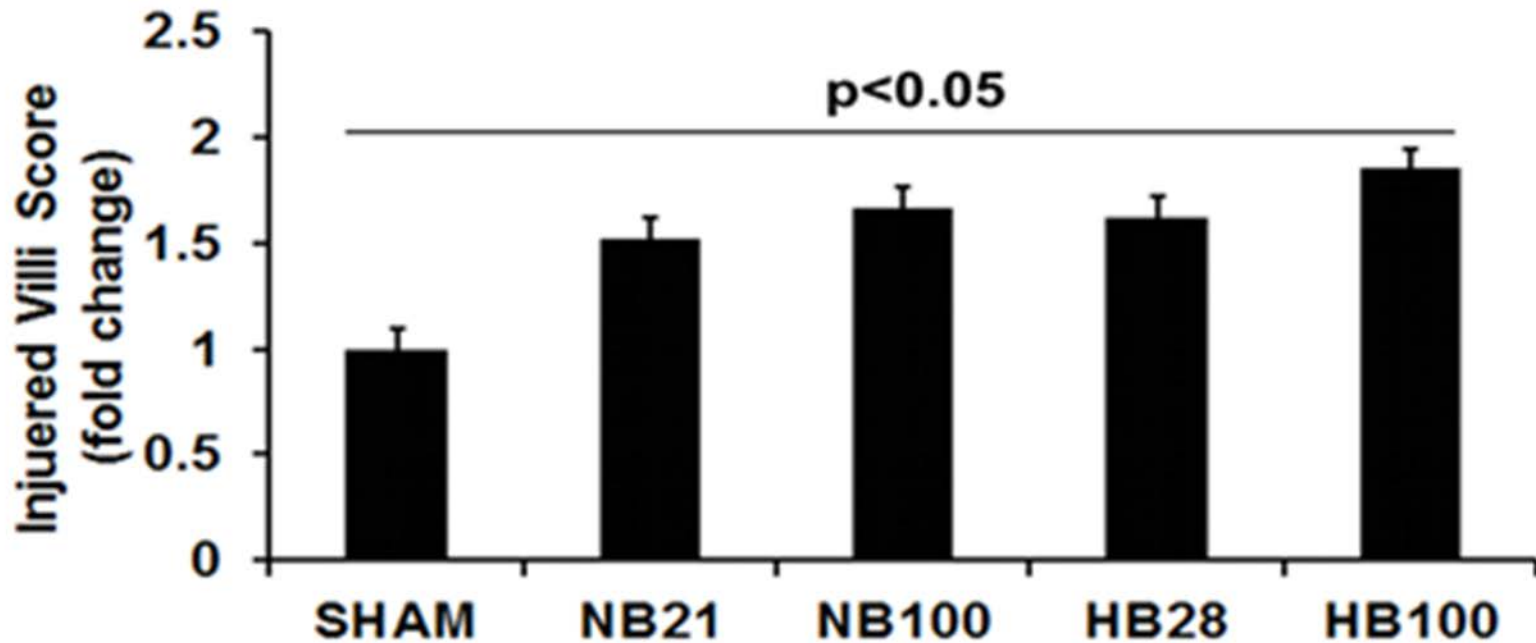


**Shock alone  
or TBI alone**



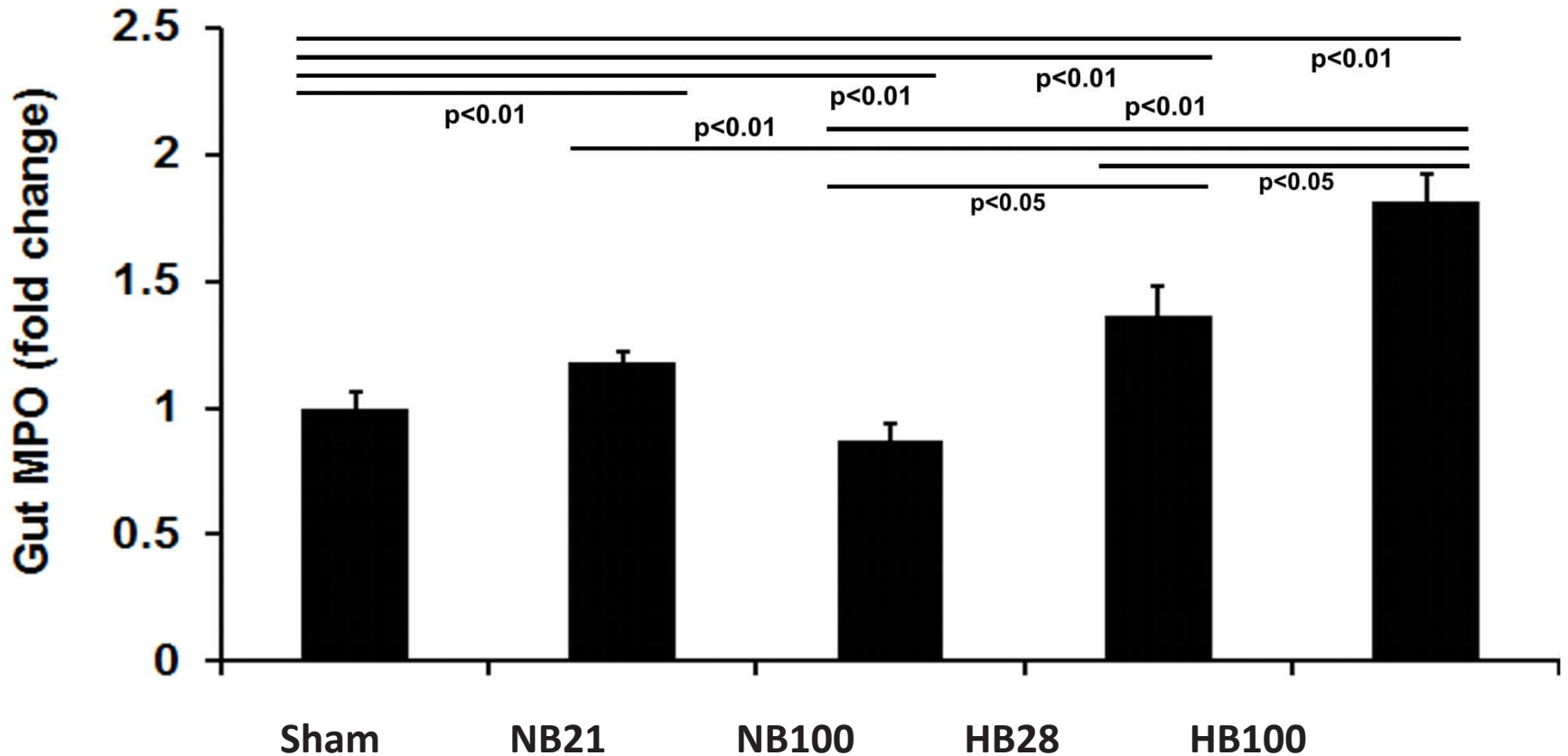
**Shock +TBI**

# GUT DAMAGE AT 30 DAYS POST-POLYTRAUMA



*Hyperoxic hypobarica worsens gut damage at 30 days post-injury*

# GUT INFLAMMATION (MYELOPEROXIDASE) 30 DAYS\_POST-POLYTRAUMA

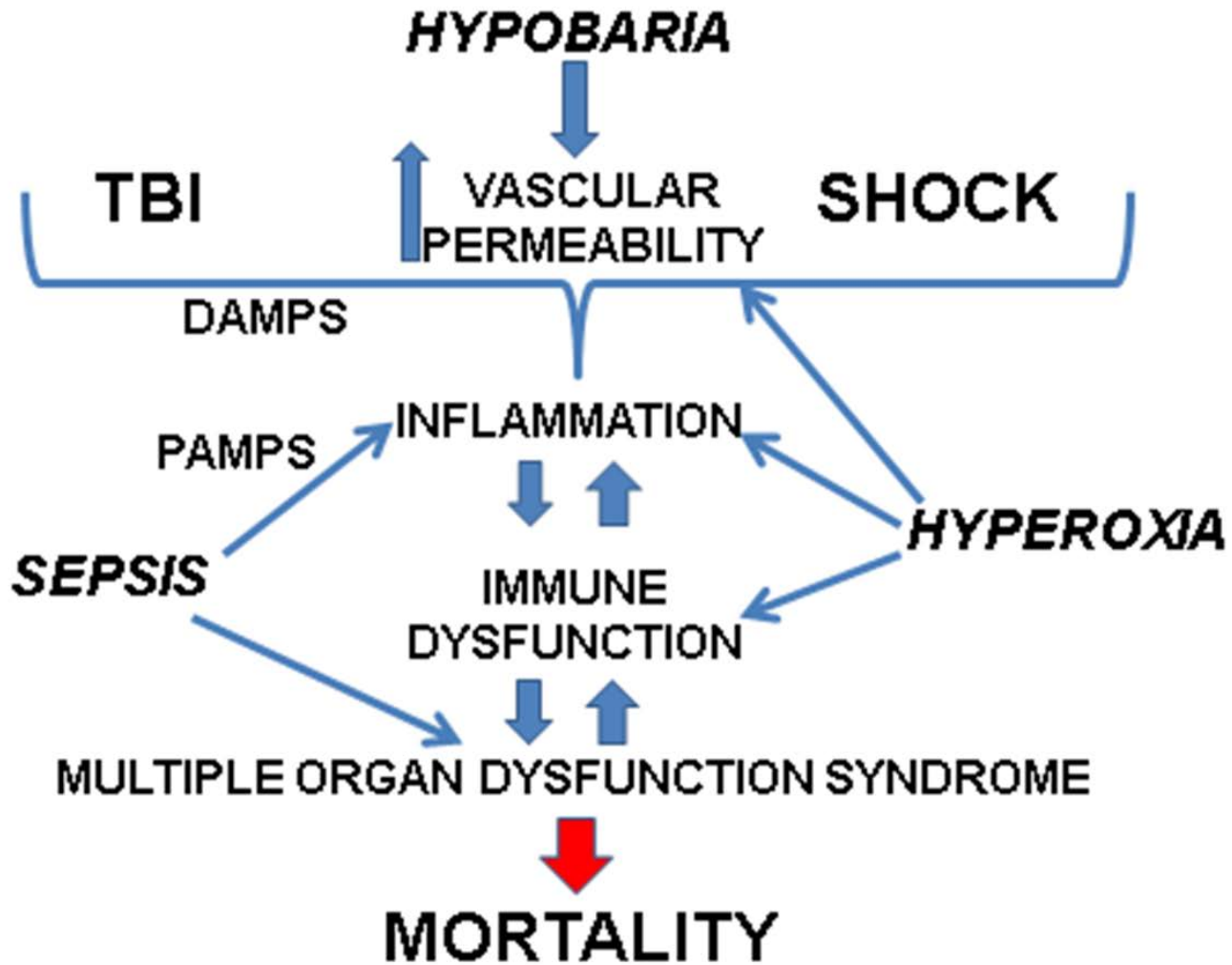


*Hyperoxic hypobaria worsens gut inflammation at 30 days post-injury*

# Conclusions

- ***The combination of TBI and shock results in substantial mortality under conditions where either alone results in little to no mortality.***
- ***Exposure to AE-relevant hypobarica at 24 hours post-trauma increases mortality.***
- ***Exposure to high (100%) oxygen can exacerbate the effects of hypobarica on mortality after polytrauma.***
- ***The effects of hypobarica and hyperoxia on mortality may be due to exacerbation of multi-organ dysfunction.***

# MECHANISMS OF MODS WORSENERD BY AE-RELEVANT HYPOBARIA



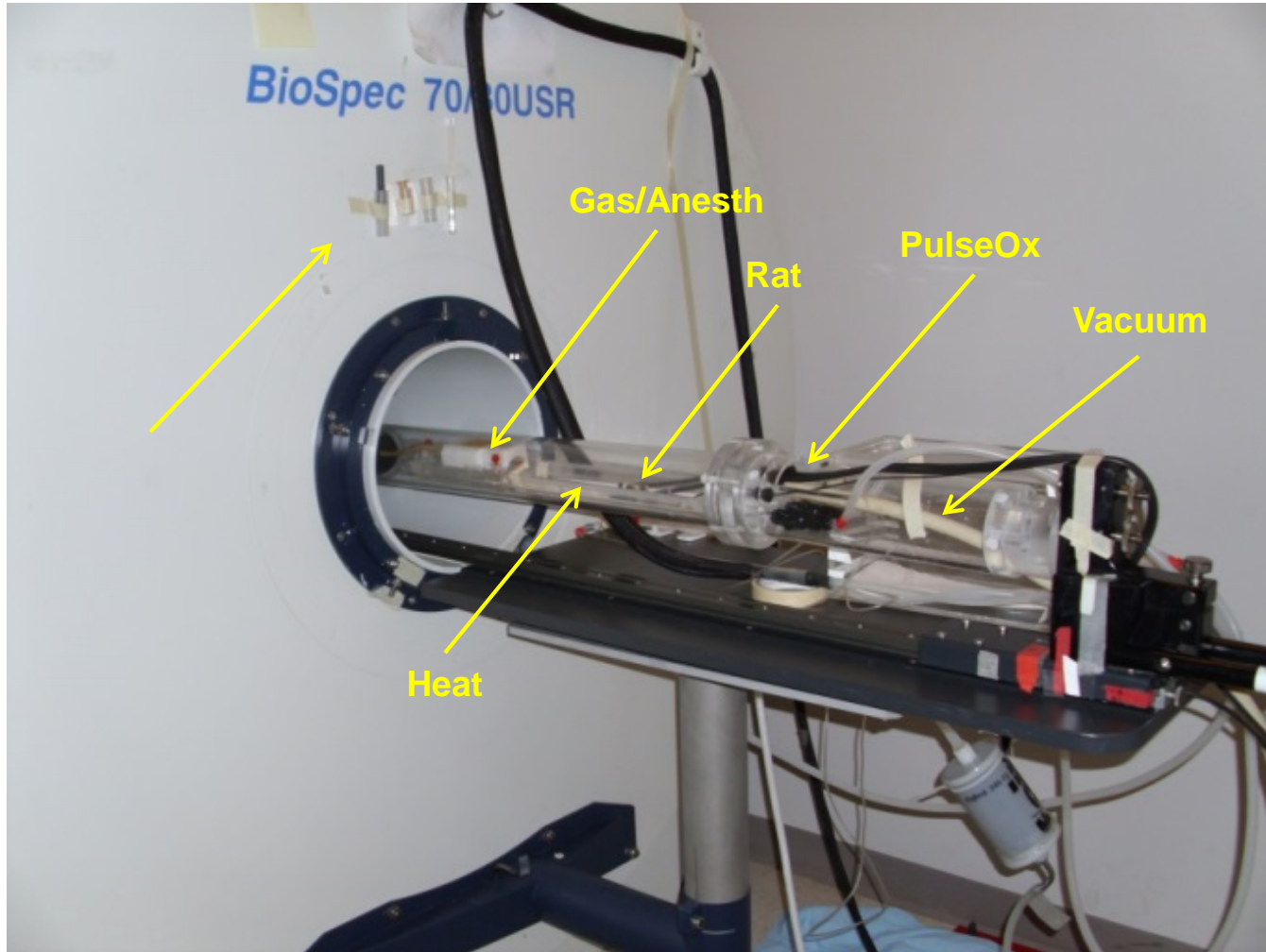


# Way Forward

- *Test for damage to other organs, e.g., heart, liver, adrenals, etc*
- *Compare effects of AE at 4000 and 8000 ft hypobaria*
- *Test for effects of multiple flights over long periods*
- *Test potential polytrauma therapeutics administered prior to and after exposure to AE-relevant hypobaria*
  - *Agents, e.g., sulforaphane , that increase anti-oxidant gene expression*
- *Determine if pre-existing stress worsens injury and exacerbates secondary injury due to hypobaria*
- *Use MRI and MRS during hypobaria to better understand how hypobaria worsens organ injury*



# HYPOBARIC CHAMBER PRESENT WITHIN THE BRUKER 7 TESLA MRI DEVICE



# Questions?