



# Development of a large animal model of hemorrhage and traumatic brain injury to simulate Prolonged Casualty Care

Ho, Jessie W<sup>1</sup>, Kemp, Michael<sup>2</sup>, Ober, Rebecca A<sup>3</sup>, Keeney-Bontrone, Toby P<sup>1</sup>, Jin, Guang<sup>1</sup>, Chtraklin, Kiril<sup>1</sup>, Latif, Zoya<sup>1</sup>, Joaquin, Theodore<sup>1</sup>, Vercruyse, Claire A<sup>1</sup>, Alam, Hasan B<sup>1</sup>

<sup>1</sup>Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, <sup>2</sup>University of Michigan, Department of Surgery, Ann Arbor, MI, <sup>3</sup>Center for Comparative Medicine, Northwestern University, Chicago, IL

## Background

- Hemorrhage and traumatic brain injury (TBI) are the leading causes of death in civilian and military settings
- Prolonged Casualty Care (PCC) is a strategic paradigm shift due to changes in future warfare
- PCC aims to deliver up to 3 days of field care prior to evacuation
- We have an established porcine model with hemorrhagic shock and TBI, this model has not been tested in the PCC setting.

## Objective

Develop a reproducible model of hemorrhagic shock and TBI to test novel therapies in PCC

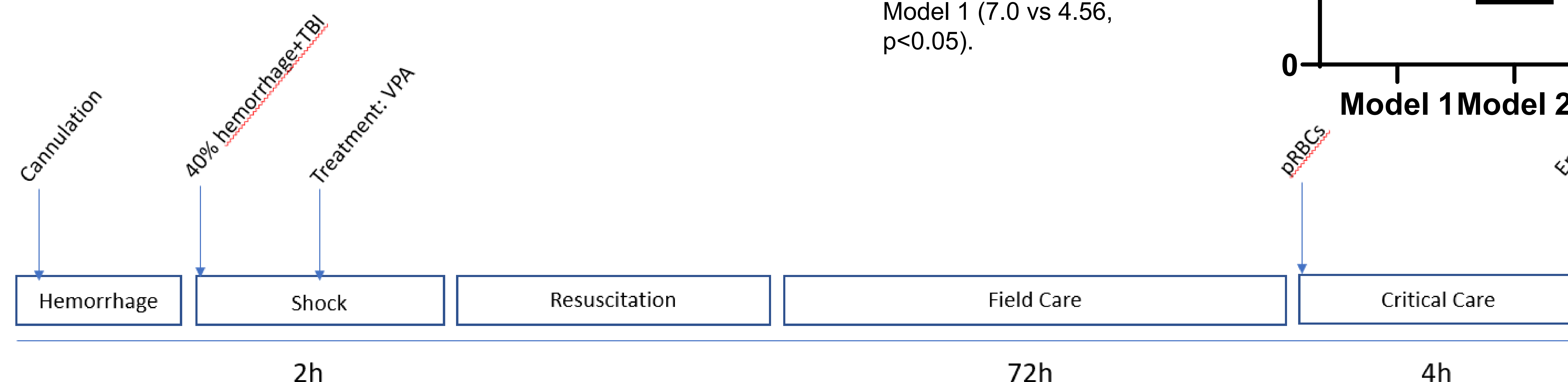
### Common goals for collaboration

1. Effectively integrate the lab into an existing infrastructure
2. Conduct safe, humane, ethical, and high-quality scientific inquiries
3. Be accountable
4. Have transparent, honest, and open communication
5. Strive for continuous improvement

**Table 1.** Common goals and recommendations for collaboration between scientists and veterinary staff<sup>1</sup>

## Methods

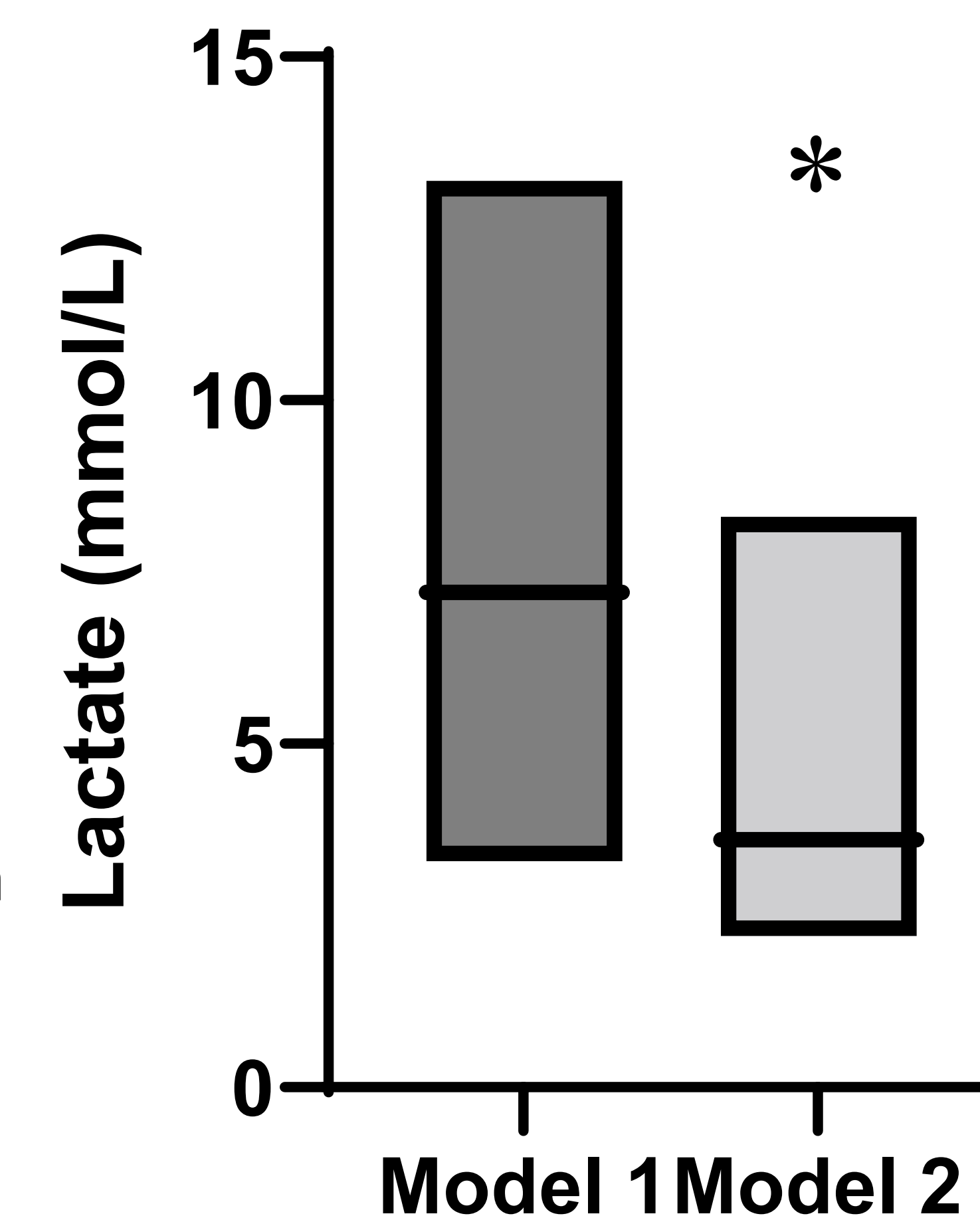
- Designed to test novel therapies
- Two models of combined hemorrhagic shock and TBI were tested (Table 2)
- Yorkshire swine, 40-45kg
- Anesthetized and instrumented
- **Damage Control Resuscitation-** controlled resuscitation with 250cc bolus over 15 min
- **Extubation criteria-**
  - Systolic blood pressure 80mmHg for 1 hour
  - Maximum fluid volume (100ml/kg)
- 72-hour observation simulating austere PCC setting
- Blood transfusion simulating transfer to higher level of care
- **End point-**76 hours
- **Outcomes-**
  1. Fluid resuscitation requirements
  2. TBI brain lesion size
  3. Neurologic Severity Score



**Figure 1.** Model 2 experimental timeline. The vessels are cannulated. An 8mm controlled cortical impact and hemorrhage occur simultaneously. During shock, the mean arterial pressure (MAP) is maintained at 30-35mmHg. During shock, the swine are randomized in to treatment or control groups. Damage control resuscitation begins following shock until defined extubation criteria occur. The pRBCs are transfused at 72 hours. The animal is euthanized at 76 hours. TBI-traumatic brain injury, VPA- valproic acid, h-hour, pRBCs-packed red blood cells.

Model 1	Model 2
50% Hemorrhage 8mm depth TBI 1hr shock (MAP goal 26-30mmHg) Resuscitation	40% Hemorrhage 8mm depth TBI 2hr shock (MAP goal 30-35mmHg) Resuscitation

**Table 2.** Trialed Models. TBI-traumatic brain injury, MAP-mean arterial pressure.



**Figure 2.** Peak lactate levels between the two groups. There is a significantly higher lactate in Model 1 (7.0 vs 4.56, p<0.05).

## Results

- Survival model requires a strong culture of collaboration with veterinary and husbandry staff (Table 1)
- Following mortality rate in Model 1, Model 2 was developed to create a severe yet survivable model
- **Mortality rates 41.7% (5/12) vs 11.1% (1/9) in Model 2**
- Model 1, 2 animals died intra-operatively, 3 died in the early-post-operative period
- Significantly higher peak lactate in Model 1 (Figure 2)
- Majority of animals (4/5) with lactate>5.5mmol at time of extubation died

## Future & Ongoing Work

- Continue work using the model to test the effects of VPA on hemorrhagic shock and TBI

## Conclusions

We have developed the first large animal model of hemorrhagic shock and TBI in a simulated PCC setting. This model is clinically relevant, reproducible, and suitable for testing novel treatments for battlefield use.

## Reference

<sup>1</sup>Ober RA, Ho JW, Kemp MT, Keeney-Bontrone TP, Geist GE, Alam HB. Culture and collaboration between the clinician-scientist and veterinary specialist: An essential interprofessional partnership in the translational sciences. *Lab Anim (NY)*. Apr 2022;51(4):95-97. doi:10.1038/s41684-022-00944-x