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UNIVERSITY OF TORONTO

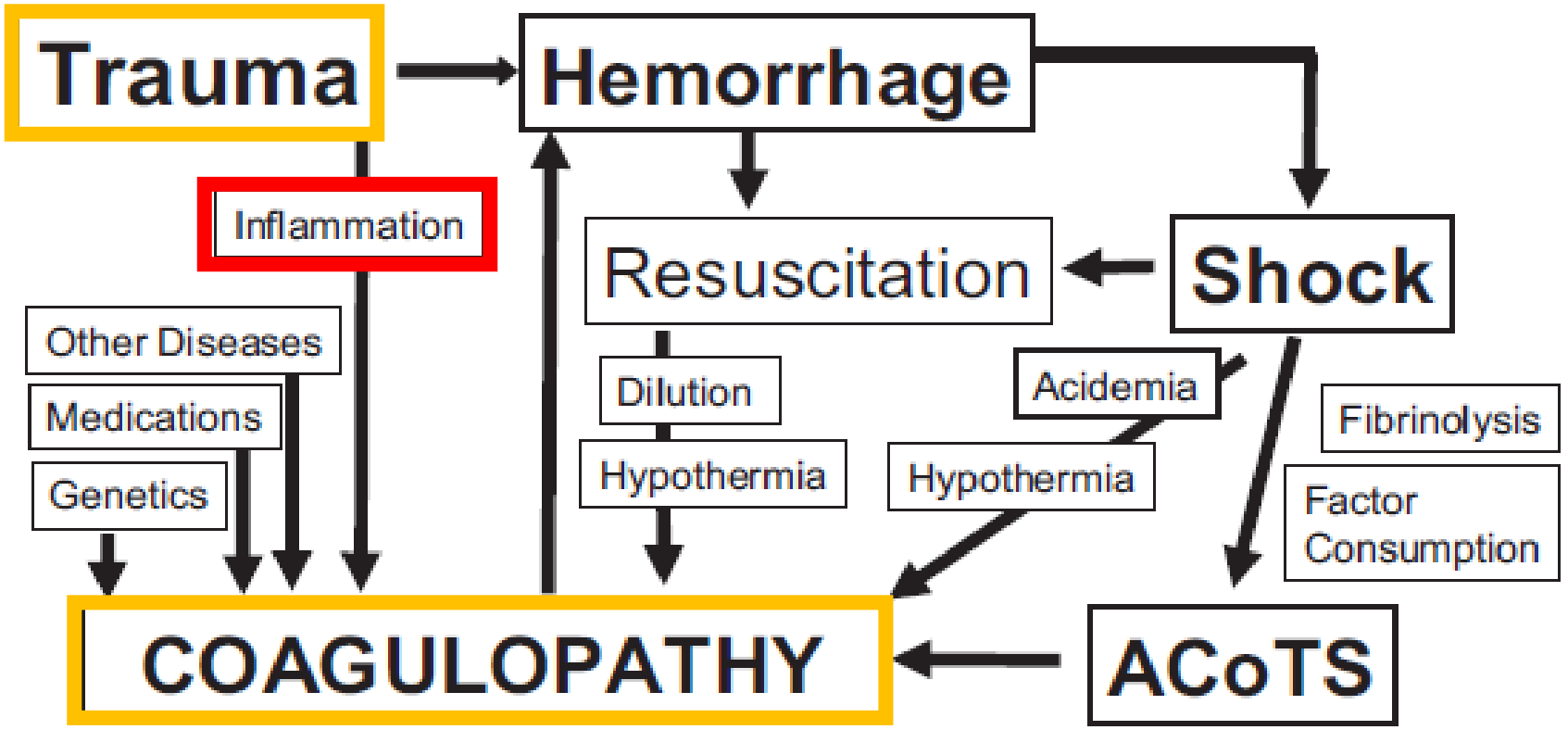
Vagal Nerve Stimulation Improves Coagulopathy in Hemorrhagic Shock: A Thromboelastometric Study in an Animal Model

Rezende-Neto JB, Lage R, Carvalho M, Almeida T, Trant C, Andrade M, Kushmerick C, Rizoli S, Melo J.

TRAUMA 2014: TRAUMA ASSOCIATION OF CANADA ANNUAL SCIENTIFIC MEETING
APR 10 & 11, 2014 THU-FRI
CENTRE MONT-ROYAL MONTREAL QC

Background

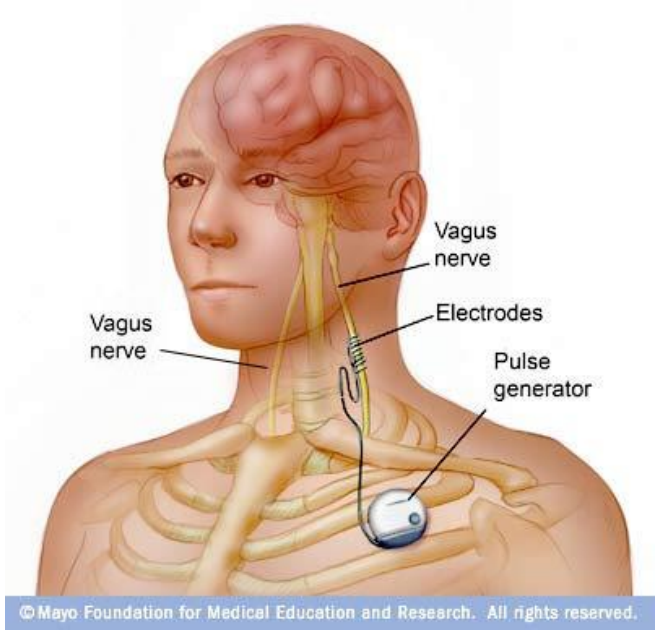
- TAC is multifactorial - inflammation plays a major role.



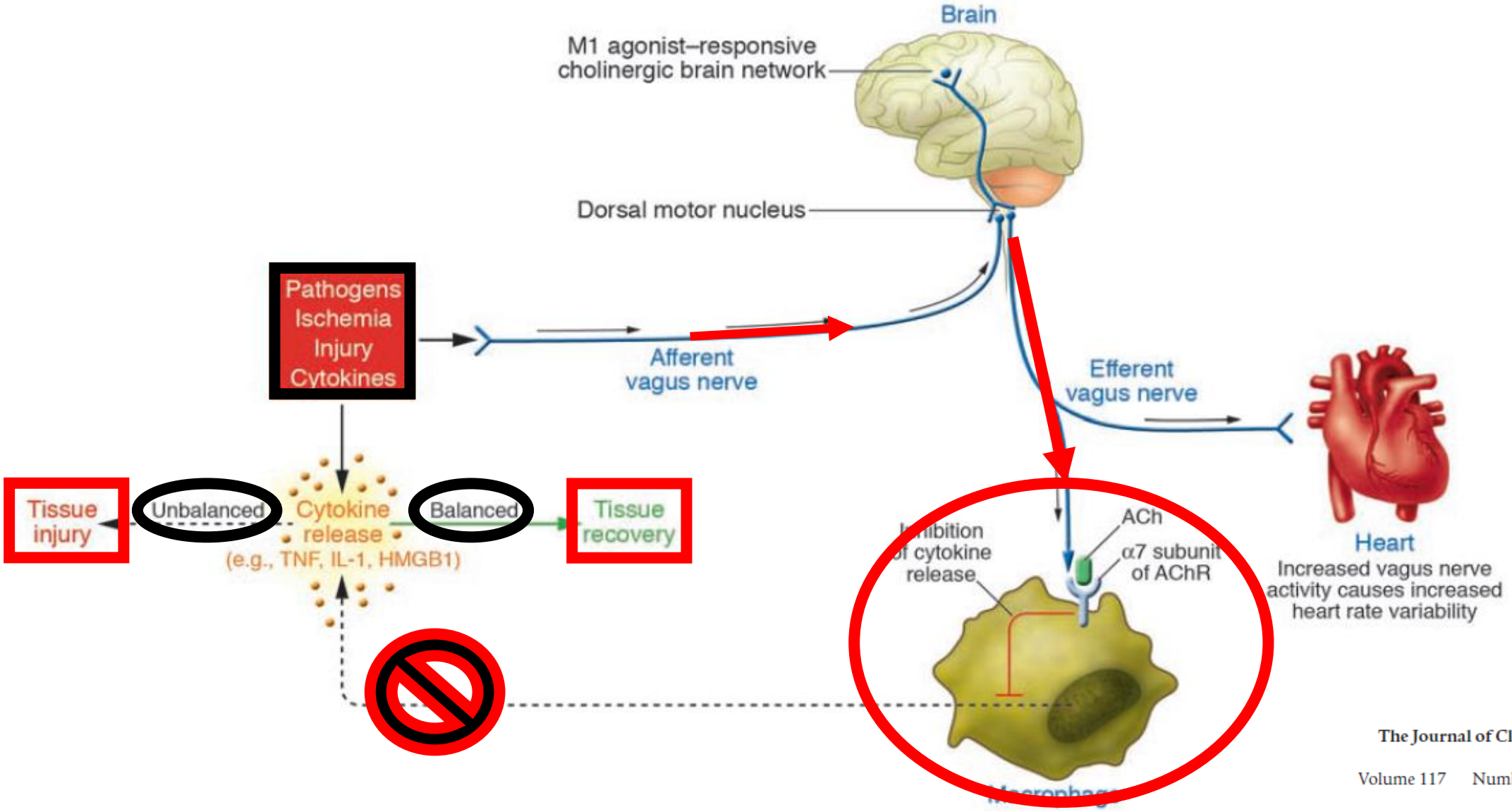
J Trauma. 2008;65:748–754.

The Central Nervous System Regulates Inflammation Via the Vagal Nerve

“THE CHOLINERGIC ANTI-INFLAMMATORY PATHWAY”

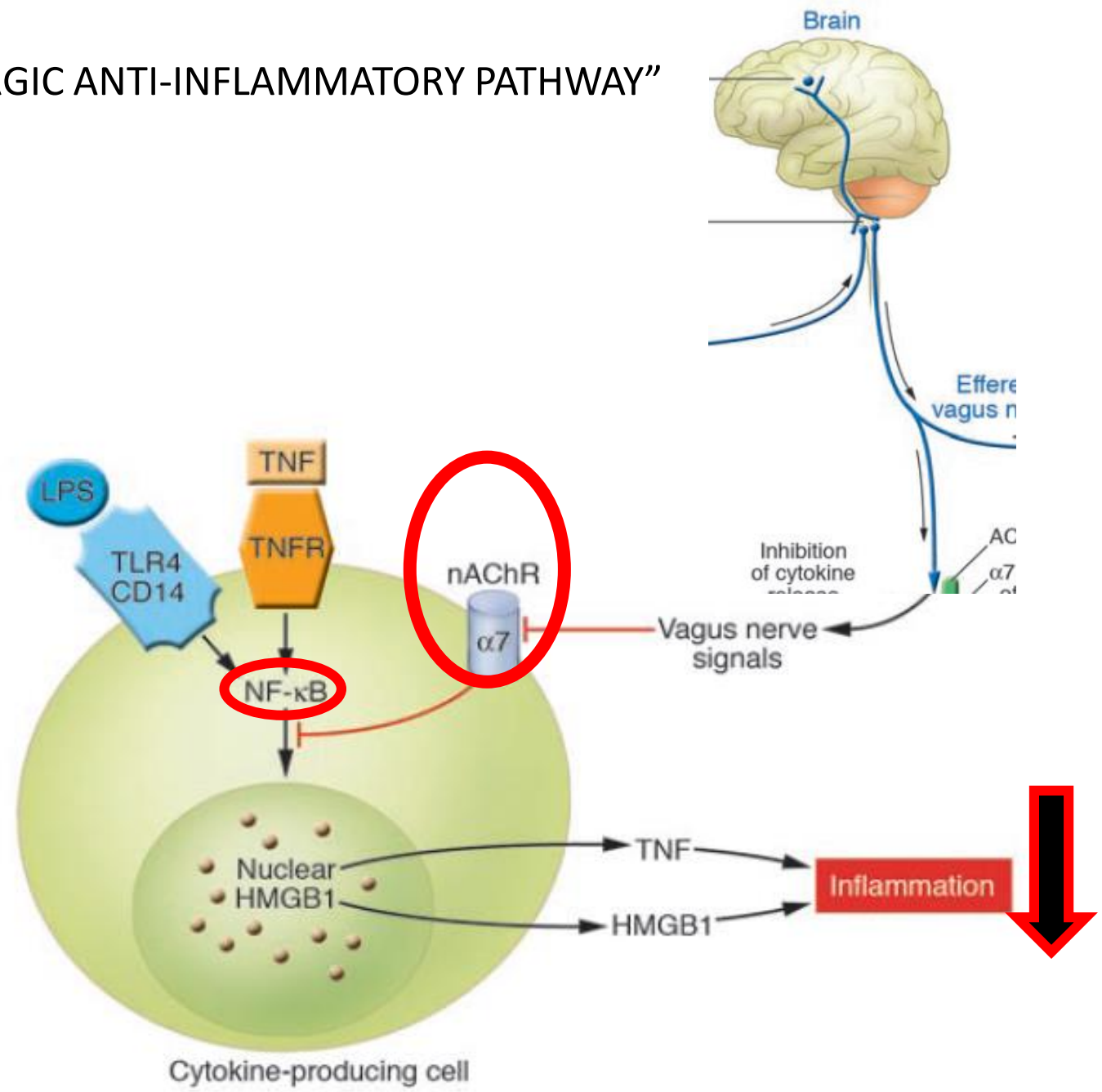


“Cholinergic Anti-Inflammatory Pathway”



The Journal of Clinical Investigation
Volume 117 Number 2 February 2007

THE CHOLINERGIC ANTI-INFLAMMATORY PATHWAY”



The Journal of Clinical Investigation
Volume 117 Number 2 February 2007

Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin

NATURE | VOL 405 | 25 MAY 2000 | www.nature.com

Neuroimmune Regulation of Ventilator-induced Lung Injury

Am J Respir Crit Care Med 2011; 183:471-481.

VAGAL NERVE STIMULATION BLOCKS PERITONEAL MACROPHAGE INFLAMMATORY RESPONSIVENESS AFTER SEVERE BURN INJURY

SHOCK, Vol. 38, No. 3, pp. 294–300, 2012

Vagal Stimulation Modulates Inflammation through a Ghrelin Mediated Mechanism in Traumatic Brain Injury

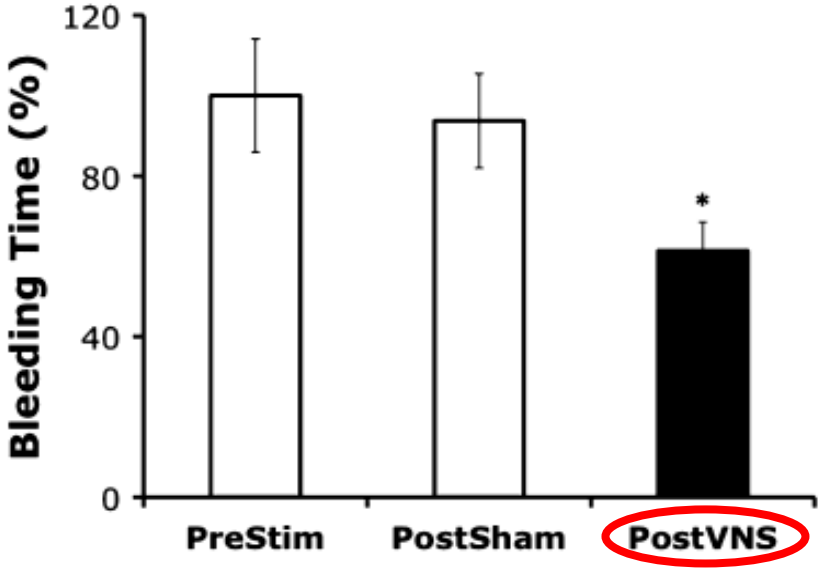
Inflammation (© 2011)
DOI: 10.1007/s10753-011-9307-7

Efferent Vagal Fibre Stimulation Blunts Nuclear Factor-κB Activation and Protects Against Hypovolemic Hemorrhagic Shock

Circulation. 2003;107:1189-1194

VAGUS NERVE STIMULATION REGULATES HEMOSTASIS IN SWINE

Christopher J. Czura,*† Arthur Schultz,‡ Martin Kaipel,‡ Anna Khadem,‡
Jared M. Huston,* Valentin A. Pavlov,* Heinz Redl,‡ and Kevin J. Tracey*†



Limitations:

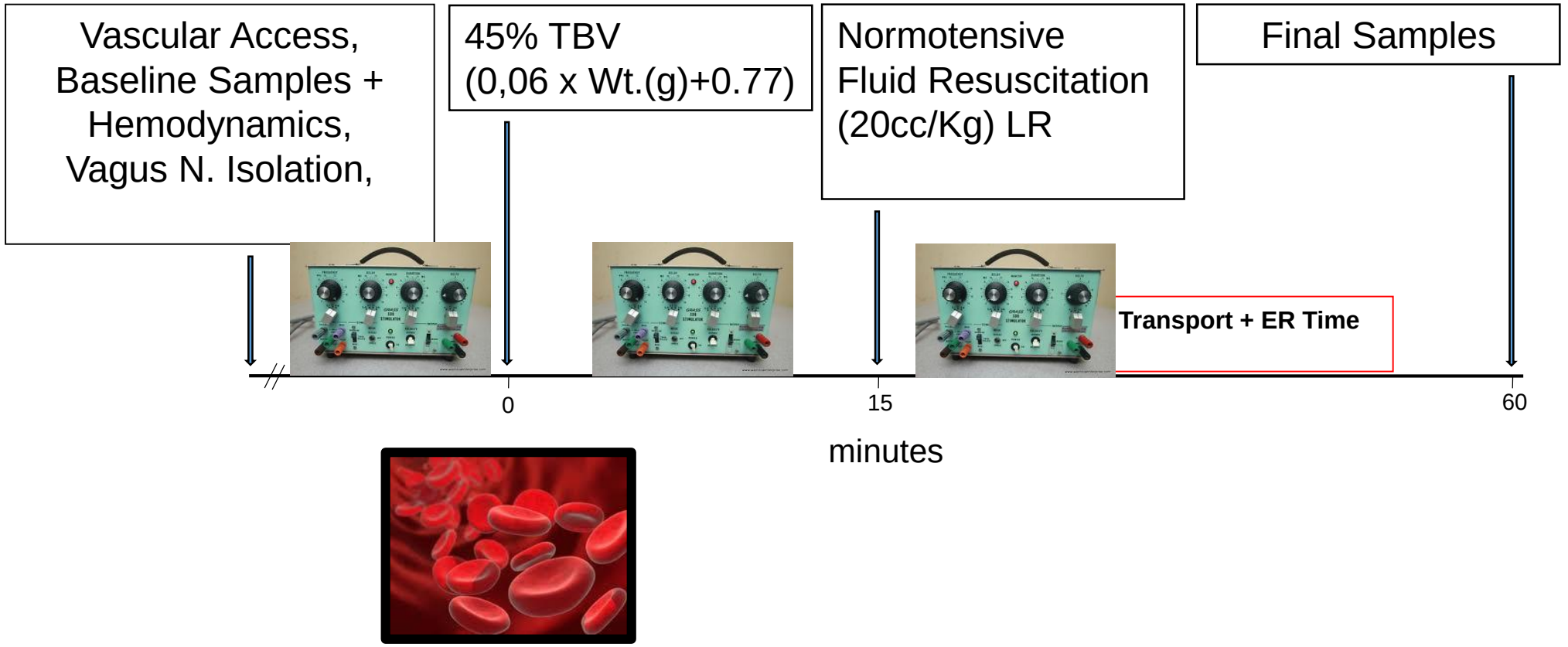
- Peripheral injury (no shock)
- VNS before hemorrhage (clinical relevance)
- Minimal fluid resuscitation (clinical relevance)

SHOCK, Vol. 33, No. 6, pp. 608–613, 2010

Hypothesis

Vagal nerve stimulation, during hemorrhagic shock resuscitation, improves coagulation.

CONTROLLED HEMORRHAGIC SHOCK MODEL



Methods

- 48 Rats
- Thromboelastometry
- Citokines (IL-1, IL-6, IL-10, TNFα)

Baseline vs. Final

Intact Vagal Nerves

- Sham
- Group 1: but no Bleed (3.5mA, 5Hz) 30s 7x
- Group 2A: Bleed + fluid resuscitation only
- Group 2B: Bleed + during fluid resuscitation
- Group 3A: followed by Bleed

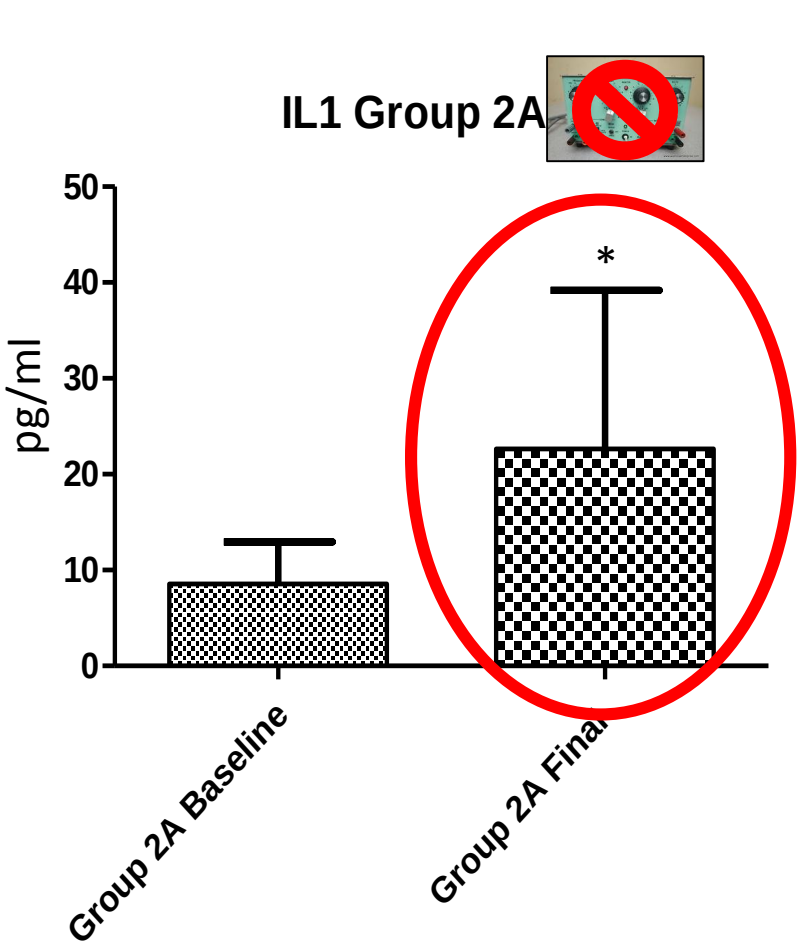
Vagotomy

- Group 3B: Bleed + Bilat. Vagotomy
- Group 4A: Bleed + Bilateral Vagotomy +

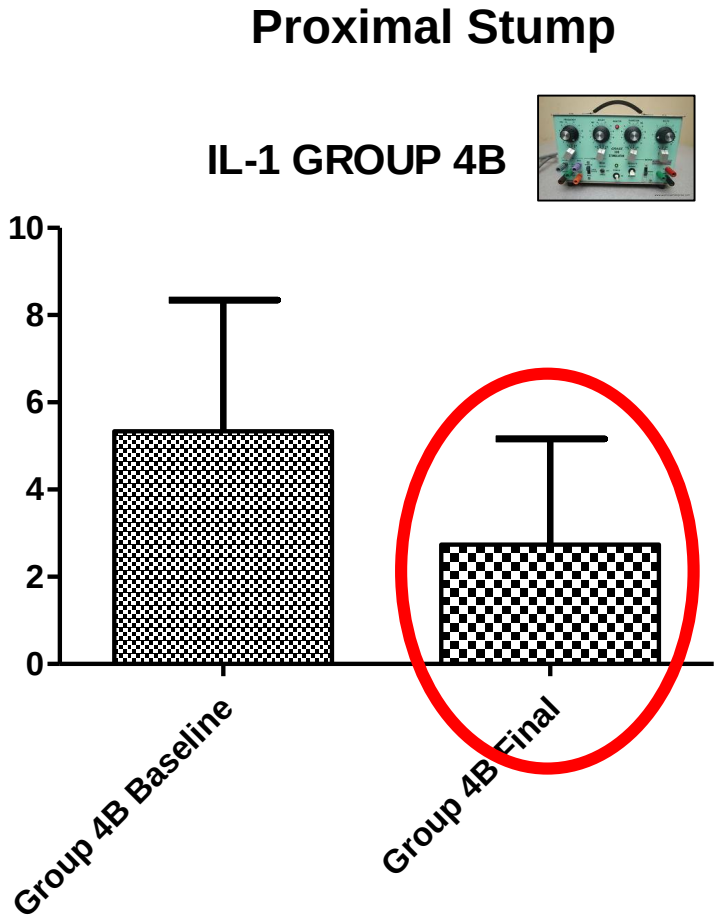
  of **Distal** Stump (during fluid resuscitation)
- Group 4B: Bleed + Bilateral Vagotomy +

  of **Proximal** Stump (during fluid resuscitation)

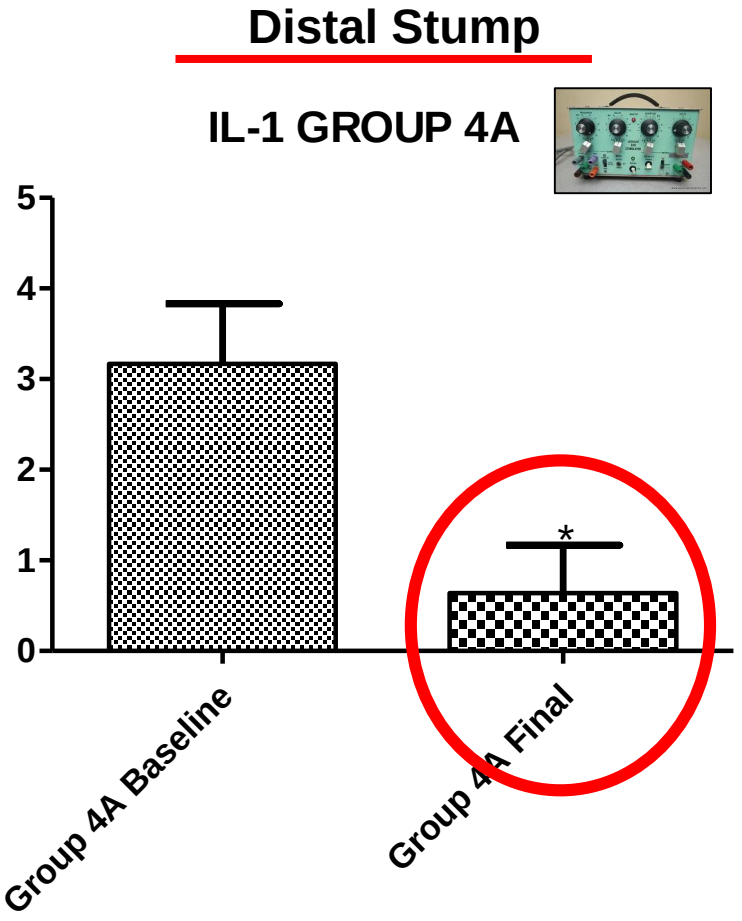
Results
Cytokine



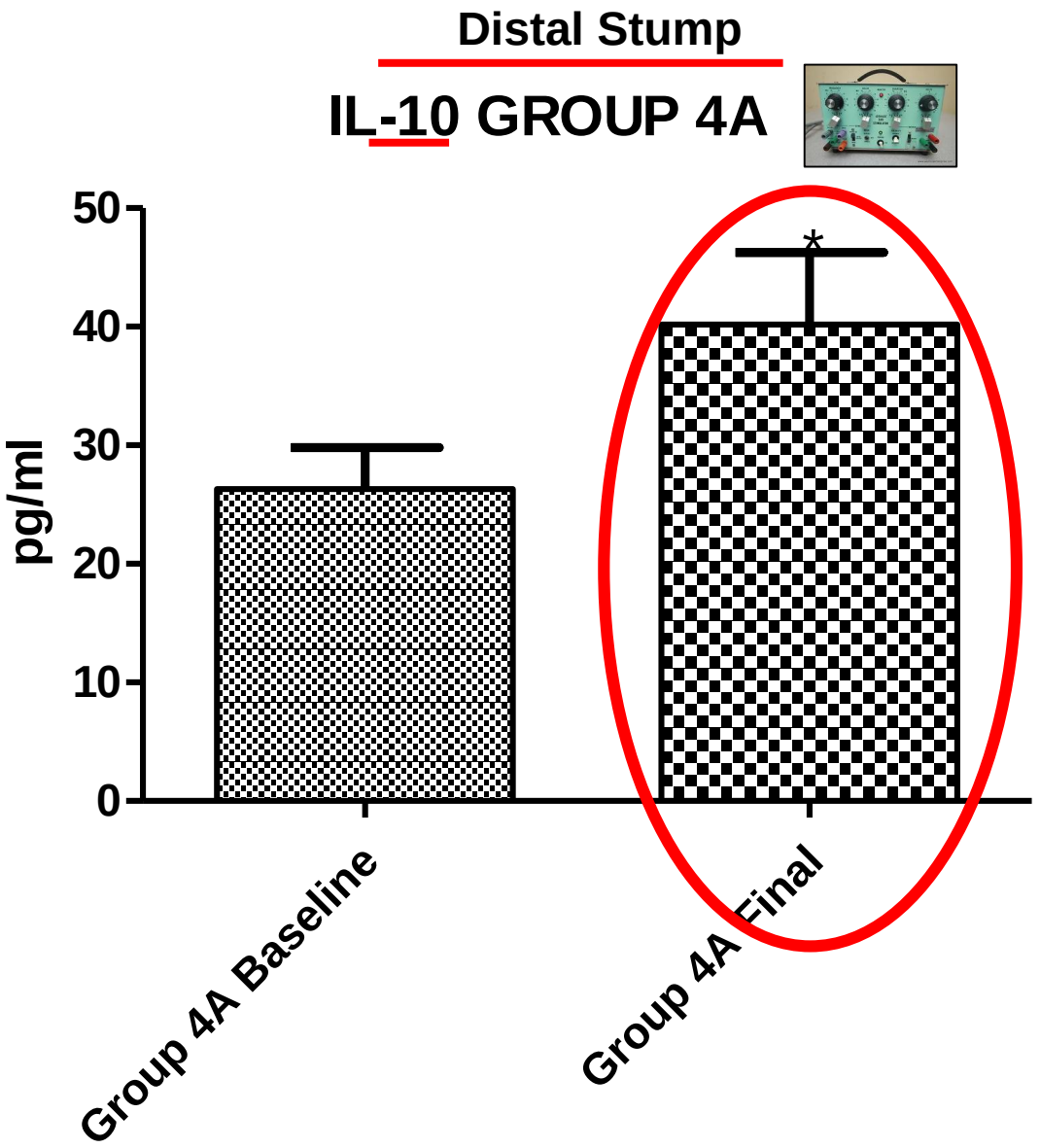
Proximal Stump



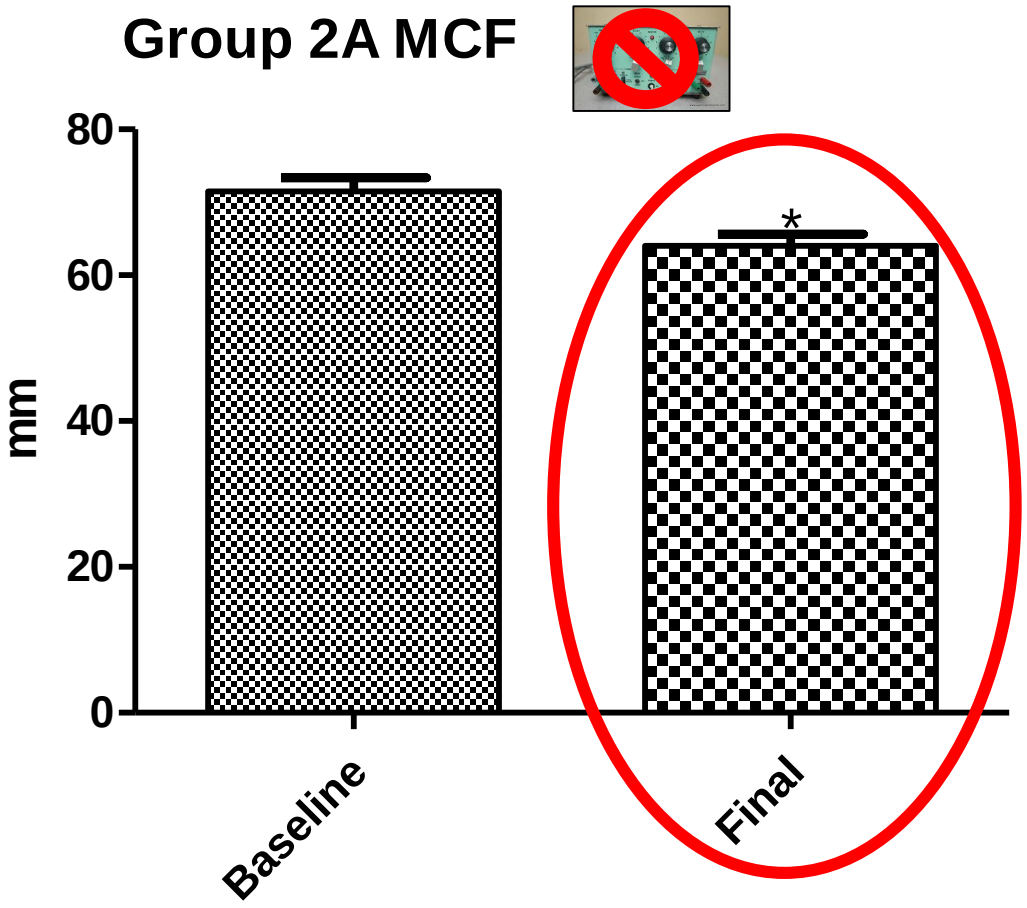
Distal Stump

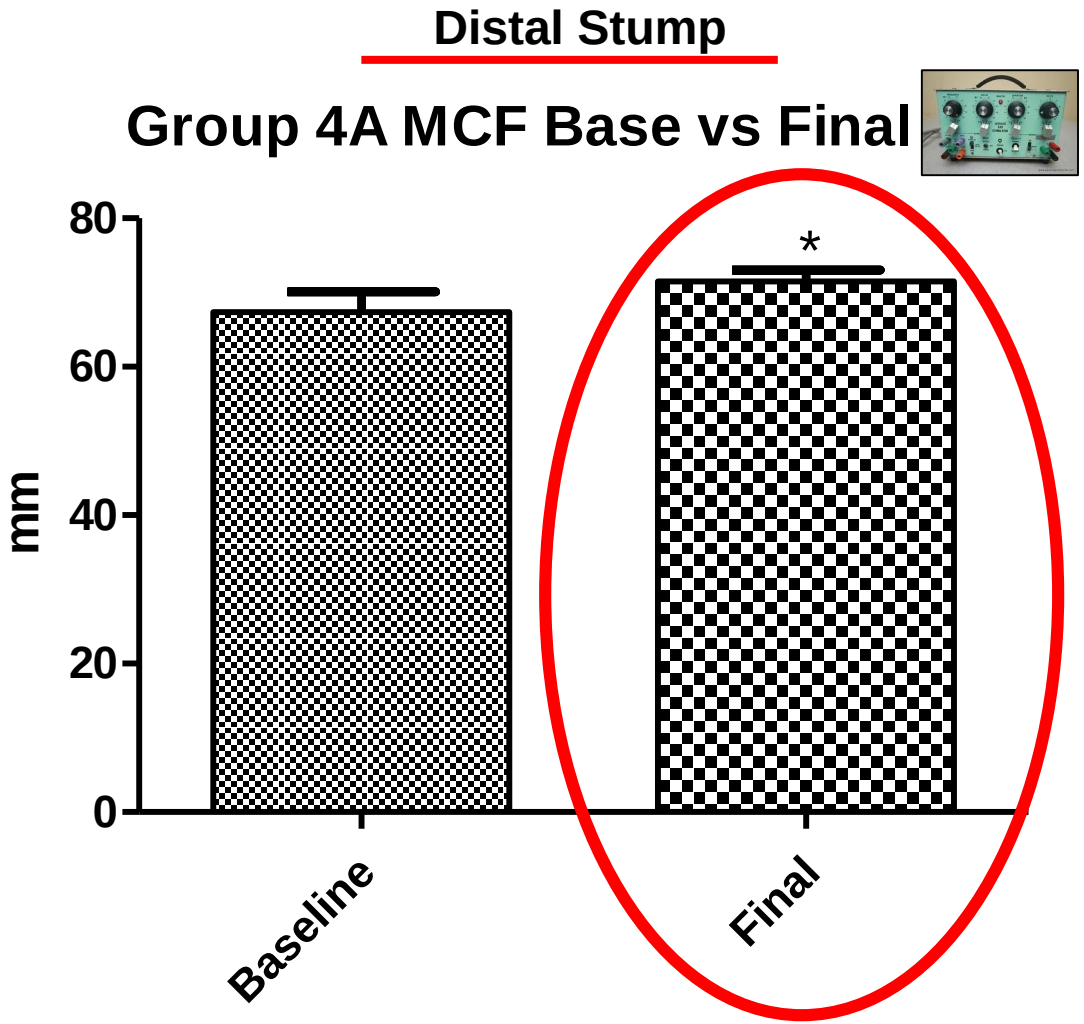


Results

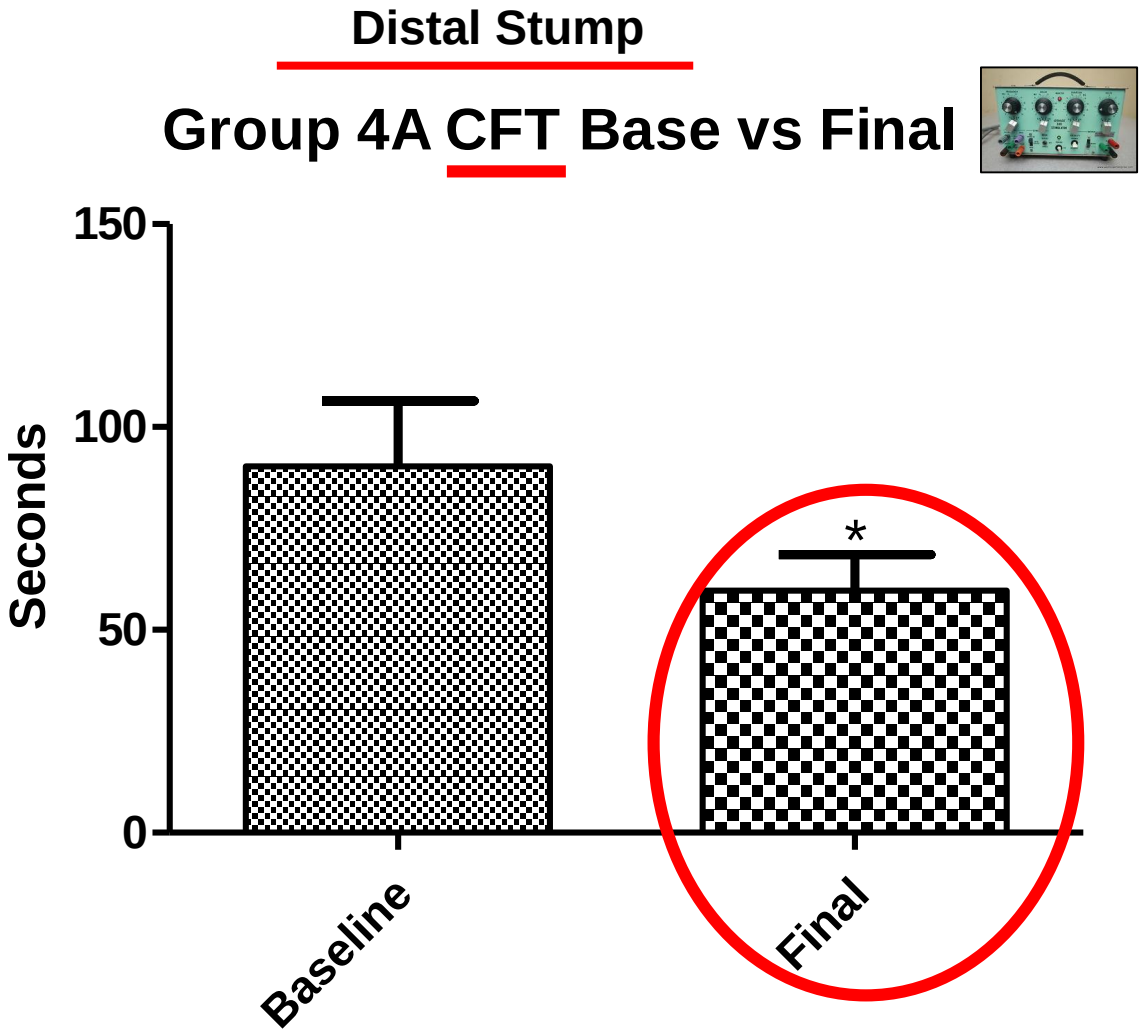

Distal Stump
IL-10 GROUP 4A
50
40
30
20
10
0
pg/ml
*
Group 4A Baseline
Group 4A Final

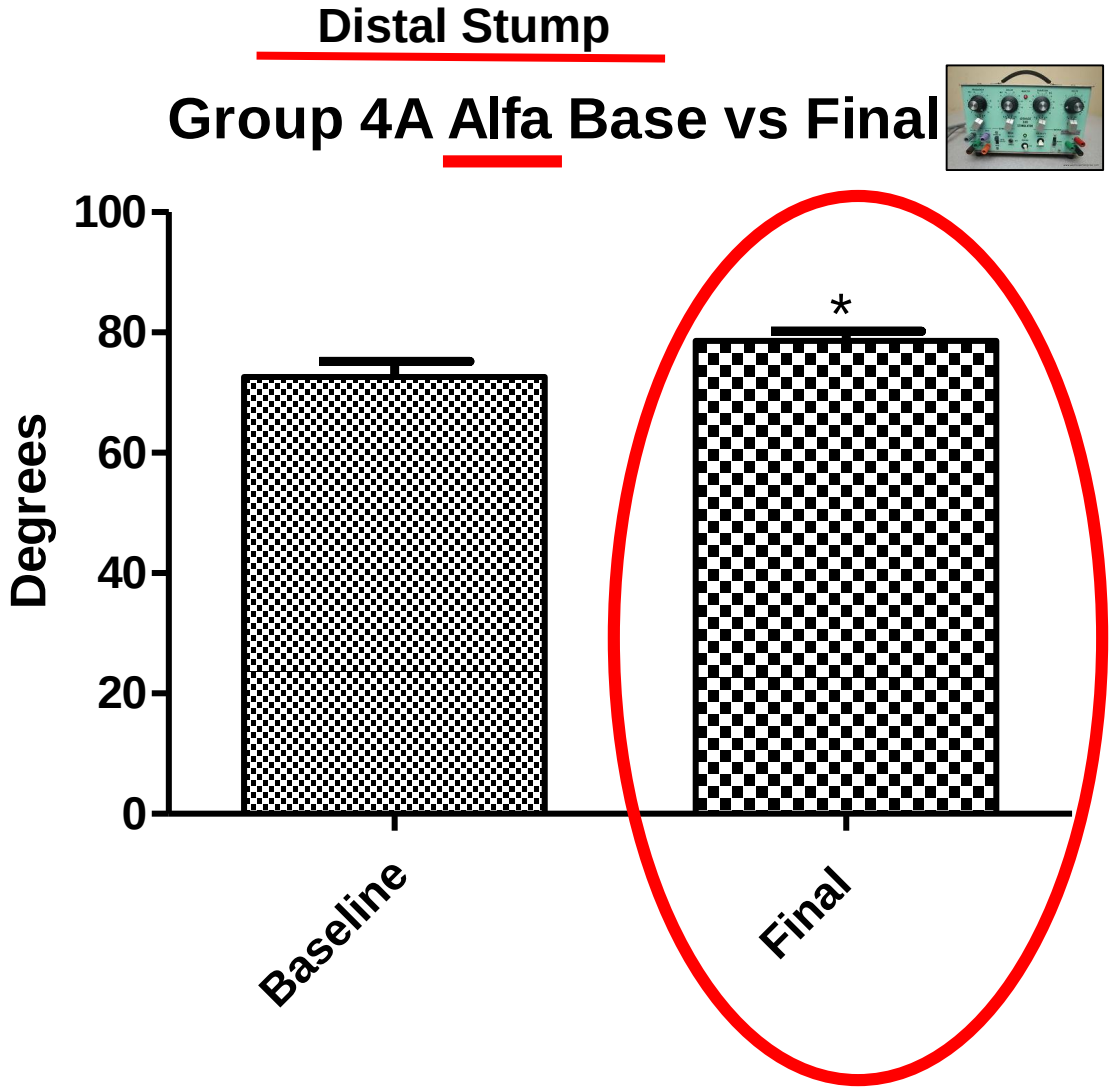
Results
Coagulation





Results


Distal Stump
Group 4A CFT Base vs Final
Seconds
150
100
50
0
*
Baseline
Final


Distal Stump
Group 4A Alfa Base vs Final
Degrees
100
80
60
40
20
0
*
Baseline
Final

Results

- Other VNS strategies failed to improved coagulation compared to baseline values.

- No difference in the hemodynamic status of hemorrhaged animals regardless of the VNS strategy used.

Conclusions

- After bilateral vagotomy…
- Efferent VNS, during resuscitation, decreases pro-inflammatory cytokine (IL-1).
- Increases anti-inflammatory cytokine (IL-10)
- Improves coagulation

THANK YOU!