What Causes Ventilator-Induced Lung Injury?

Brian Kavanagh
Hospital for Sick Children
University of Toronto
A completely biased and incomplete account of mechanisms of VILI from a single lab...

Brian Kavanagh

Hospital for Sick Children
University of Toronto
Conflicts of Interest

No financial conflict of interest with the subject matter of this talk
Atelectasis

Does Atelectasis matter?
Atelectasis Causes Vascular Leak and Lethal Right Ventricular Failure in Uninjured Rat Lungs

Michelle Duggan, Conán L. McCaul, Patrick J. McNamara, Doreen Engelberts, Cameron Ackerley, and Brian P. Kavanagh

Before Recruitment

Am J Respir Crit Care Med 2003
Atelectasis Causes Vascular Leak and Lethal Right Ventricular Failure in Uninjured Rat Lungs

Michelle Duggan, Conán L. McCaul, Patrick J. McNamara, Doreen Engelberts, Cameron Ackerley, and Brian P. Kavanagh

After Recruitment

Am J Respir Crit Care Med 2003
Atelectasis Causes Alveolar Injury in Nonatelectatic Lung Regions

Shinya Tsuchida, Doreen Engelberts, Vanya Peltekova, Natalie Hopkins, Helena Frndova, Paul Babyn, Colin McKerlie, Martin Post, Paul McLoughlin, and Brian P. Kavanagh

Control

Recruited

Atelectatic

AJRCCM, 2006
Atelectasis Causes Alveolar Injury in Nonatelectatic Lung Regions

Shinya Tsuchida, Doreen Engelberts, Vanya Peltekova, Natalie Hopkins, Helena Frndova, Paul Babyn, Colin McDermon, Martin Post, Paul McLoughlin, and Brian P. Kavanagh
CT - Scan

PET - Scan

End-expiration

End-inspiration

EELV_{normally-aerated}

Vt_{normally-aerated}

Bellani et al, AJRCCM 2011
Mediators

Do mediators matter?
Adverse Ventilatory Strategy Causes Pulmonary-to-Systemic Translocation of Endotoxin

DAMIAN B. MURPHY, NUALA CREGG, LORRAINE TREMBLAY, DOREEN ENGELBERTS, JOHN G. LAFFEY, ARTHUR S. SLUTSKY, ALEX ROMASCHIN, and BRIAN P. KAVANAGH

Am J Respir Crit Care Med 2000
Lung-derived soluble mediators are pathogenic in ventilator-induced lung injury

Thomas Jaecklin,1 Doreen Engelberts,1 Gail Otulakowski,1 Hugh O'Brodovich,3 Martin Post,1 and Brian P. Kavanagh1,2
Lung-derived soluble mediators are pathogenic in ventilator-induced lung injury

Thomas Jaecklin,¹ Doreen Engelberts,¹ Gail Otulakowski,¹ Hugh O’Brodovich,³ Martin Post,¹ and Brian P. Kavanagh¹,²
Lung-derived soluble mediators are pathogenic in ventilator-induced lung injury

Thomas Jaecklin,¹ Doreen Engelberts,¹ Gail Otulakowski,¹ Hugh O’Brodovich,³ Martin Post,¹ and Brian P. Kavanagh¹,²

Perfusate Donors

Perfusate

Source

Fresh Perfusate

Low \( V_T \)

Recirculating

High \( V_T \)

Recirculating
Lung-derived soluble mediators are pathogenic in ventilator-induced lung injury

Thomas Jaecklin,1 Doreen Engelberts,1 Gail Otulakowski,1 Hugh O’Brodovich,3 Martin Post,1 and Brian P. Kavanagh1,2
Genes

Do genes matter?
Early Changes in Lung Gene Expression due to High Tidal Volume

Ian B. Copland, Brian P. Kavanagh, Doreen Engelberts, Colin McKerlie, Jaques Belik, and Martin Post
Early Changes in Lung Gene Expression due to High Tidal Volume

Ian B. Copland, Brian P. Kavanagh, Doreen Engelberts, Colin McKeirle, Jaques Belik, and Martin Post

Am J Respir Crit Care Med 2003
Early growth response factor-1 in acute lung injury

Nicola Ngiam,1,2,6 Martin Post,1,4 and Brian P. Kavanagh1,2,3,4,5
Early Growth Response-1 Worsens Ventilator-induced Lung Injury by Up-Regulating Prostanoid Synthesis

Nicola Ngiam1*, Vanya Peltekova1*, Doreen Engelberts1*, Gail Otulakowski1, Martin Post1, and Brian P. Kavanagh1,2,3

1Physiology and Experimental Medicine, 2Department of Critical Care Medicine, and 3Department of Anesthesia, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

Low $V_T$  

High $V_T$  

Am J Respir Crit Care Med, 2010
What happens if we **delete** the Egr1 gene?
Early Growth Response-1 Worsens Ventilator-induced Lung Injury by Up-Regulating Prostanoid Synthesis

Nicola Ngiam, Vanya Peltekova, Doreen Engelberts, Gail Otulakowski, Martin Post, and Brian P. Kavanagh

1Physiology and Experimental Medicine, 2Department of Critical Care Medicine, and 3Department of Anesthesia, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

**Product of PGE Synthase (PGE$_2$)**

![Graph showing PGE2 levels in Egr1$^{+/+}$ and Egr1$^{-/-}$ mice with and without ventilation.](image)
Early Growth Response-1 Worsens Ventilator-induced Lung Injury by Up-Regulating Prostanoid Synthesis

Nicola Ngiam¹*, Vanya Peltekova¹*, Doreen Engelberts¹*, Gail Otulakowski¹, Martin Post¹, and Brian P. Kavanagh¹,²,³

¹Physiology and Experimental Medicine, ²Department of Critical Care Medicine, and ³Department of Anesthesia, Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

Compliance Impairment

Control: No Blocker
Age

Does *age* matter?
High Tidal Volume Ventilation Causes Different Inflammatory Responses in Newborn versus Adult Lung

Ian B. Copland, Francisco Martinez, Brian P. Kavanagh, Doreen Engelberts, Colin McKerlie, Jaques Belik, and Martin Post

Mediator Responses

Adult > Infant
Lung Development and Susceptibility to Ventilator-induced Lung Injury

Alik Kornecki, Shinya Tsuchida, Hari Kumar Ondiveeran, Doreen Engelberts, Helena Frndova, A. Keith Tanswell, Martin Post, Colin Mckerlie, Jaques Belik, Alison Fox-Robichaud, and Brian P. Kavanagh
Lung Development and Susceptibility to Ventilator-induced Lung Injury

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Adult

Expiration

Inspiration
It’s official
Thank you ...