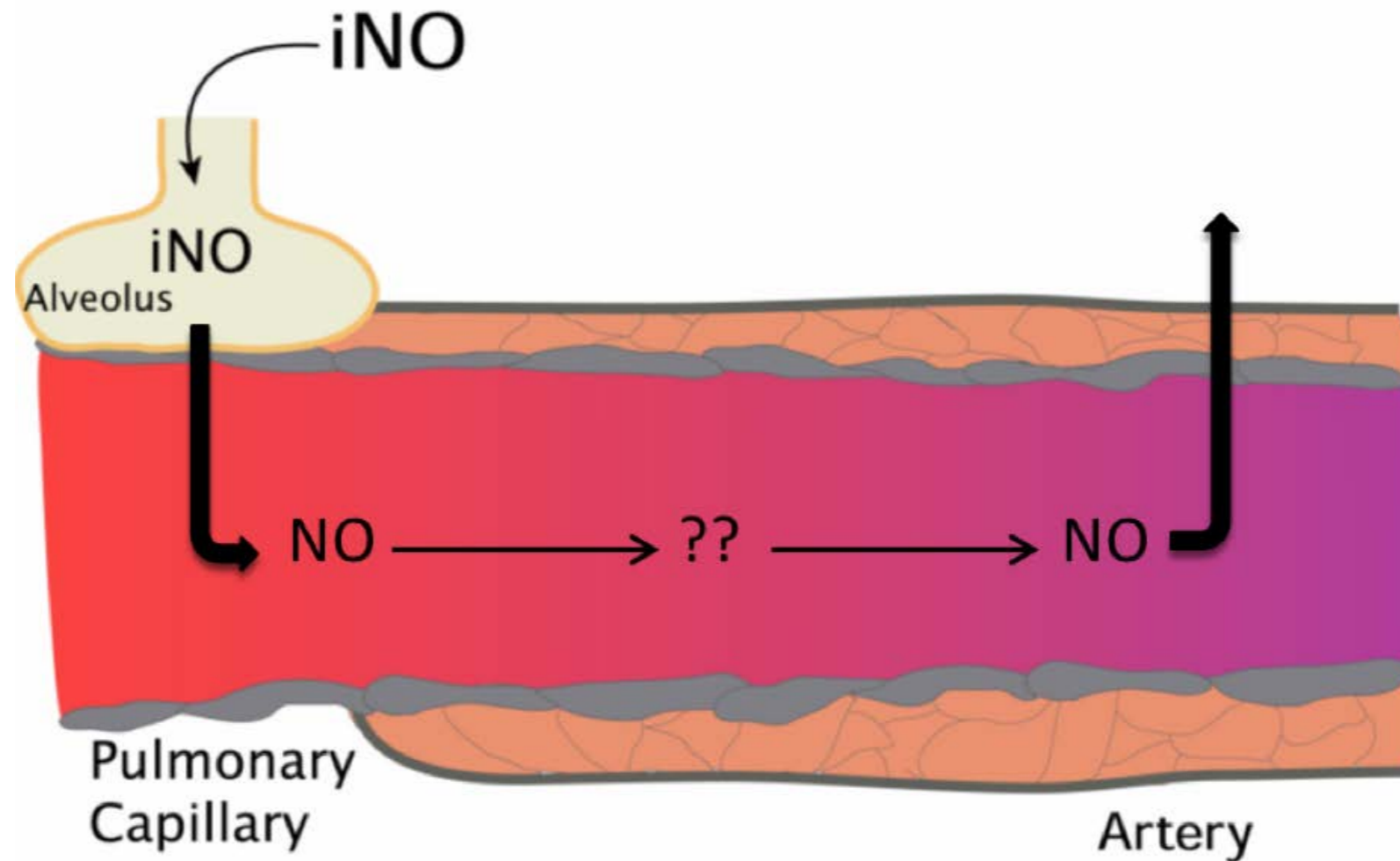


Nitric oxide metabolites; no end to NO



Arlin B. Blood, PhD

Associate Professor

Department of Pediatrics

Division of Neonatology

Center for Perinatal Biology

Loma Linda University School of Medicine



Loma Linda University
Children's Hospital

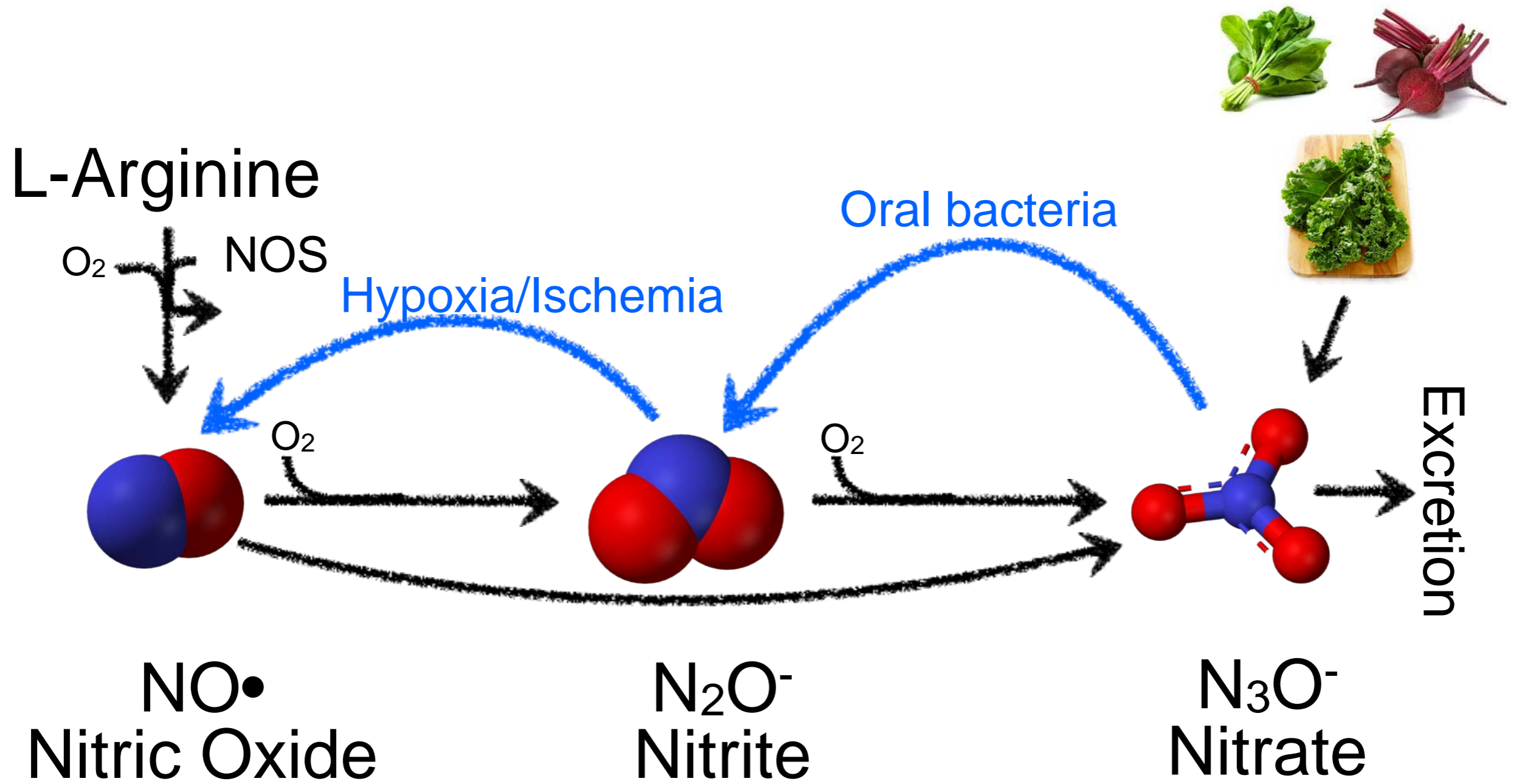
Background

- Pharmaceutical early-phase clinical trial industry
- PhD from the Center for Perinatal Biology 2003
- Member of Division of Neonatology, Department of Pediatrics since 2006
- Joined the Center for Perinatal Biology in 2008

Roles

- Mentor and facilitate research within the Neonatology fellowship program
 - 3 new fellows / year, 3-year fellowship
- Facilitate research within the Division of Neonatology and Department of Pediatrics
- Maintain a productive basic science research lab
- Teach physiology

NO metabolism



Cardiovascular effects of nitrite and nitrate

- Increased exercise performance
- Decreased oxygen consumption per work output
- Decreased blood pressure
- Increased hypoxia/ischemia tolerance
- Decreased body weight, triglycerides, visceral fat

Free Radic Biol Med. 2010 Jan 15;48(2):342-7. doi: 10.1016/j.freeradbiomed.2009.11.006. Epub 2009 Nov 12.

Dietary nitrate reduces maximal oxygen consumption while maintaining work performance in maximal exercise.

Larsen FJ¹, Weitzberg E, Lundberg JO, Ekblom B.

⊖ Author information

¹Department of Physiology and Pharmacology, Swedish School of Sport and Health Sciences, Karolinska Institutet, 11486 Stockholm, Sweden.

Dietary Inorganic Nitrate Improves Mitochondrial Efficiency in Humans

Cell
PRESS

Filip J. Larsen,^{1,2,3,*} Tomas A. Schiffer,^{1,3} Sara Borniquel,¹ Kent Sahlin,^{1,2} Björn Ekblom,^{1,2} Jon O. Lundberg,¹ and Eddie Weitzberg^{1,*}

Acute Blood Pressure Lowering, Vasoprotective, and Antiplatelet Properties of Dietary Nitrate via Bioconversion to Nitrite

Andrew J. Webb, Nakul Patel, Stavros Loukogeorgakis, Mike Okorie, Zainab Aboud, Shivani Misra, Rahim Rashid, Philip Miall, John Deanfield, Nigel Benjamin, Raymond MacAllister, Adrian J. Hobbs and Amrita Ahluwalia
Hypertension 2008;51:784-790; originally published online Feb 4, 2008;

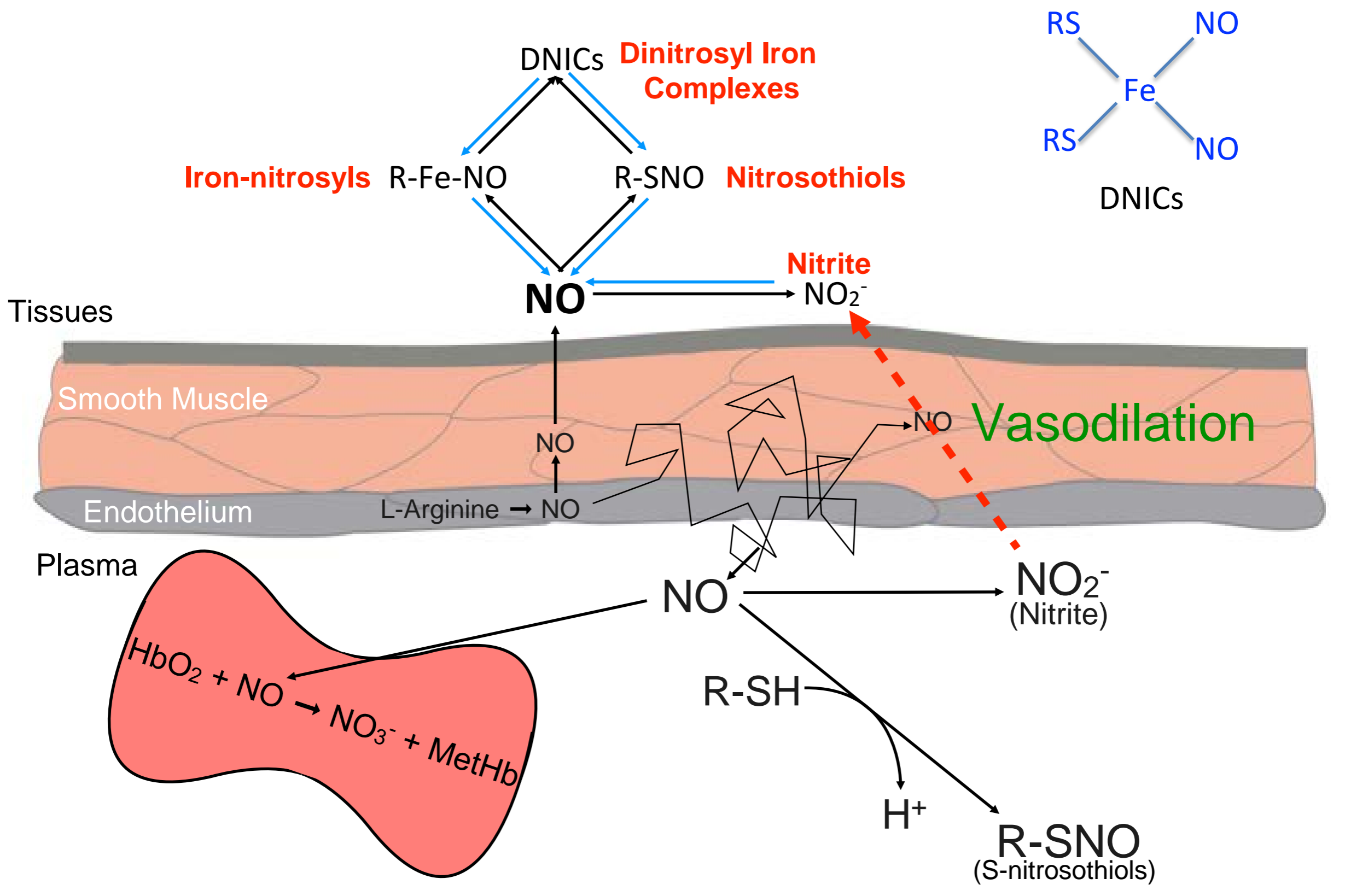
Cytoprotective effects of nitrite during in vivo ischemia-reperfusion of the heart and liver

Mark R. Duranski,¹ James J.M. Greer,¹ Andre Dejam,² Sathya Jaganmohan,¹ Neil Hogg,³ William Langston,⁴ Rakesh P. Patel,⁵ Shaw-Fang Yet,⁶ Xunde Wang,^{7,8} Christopher G. Kevil,⁴ Mark T. Gladwin,^{7,8} and David J. Lefer¹
The Journal of Clinical Investigation <http://www.jci.org> Volume 115 Number 5 May 2005

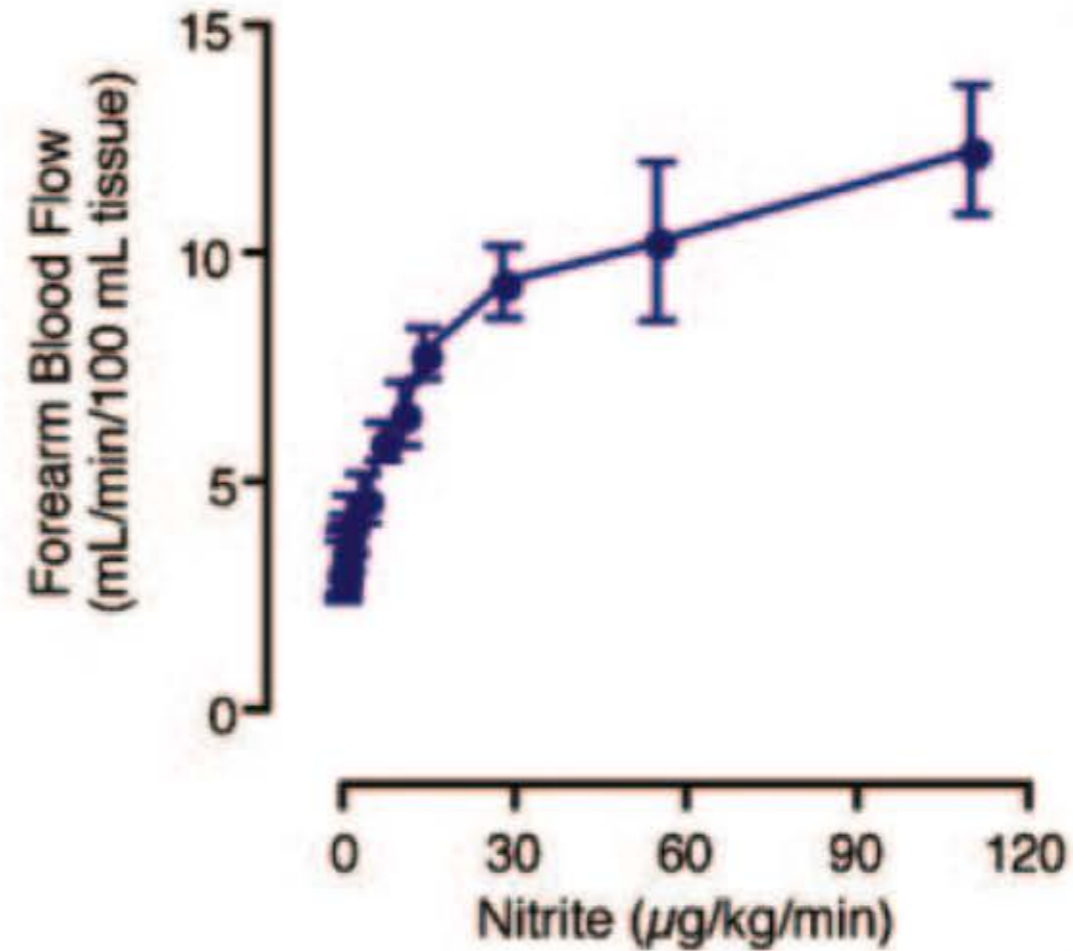
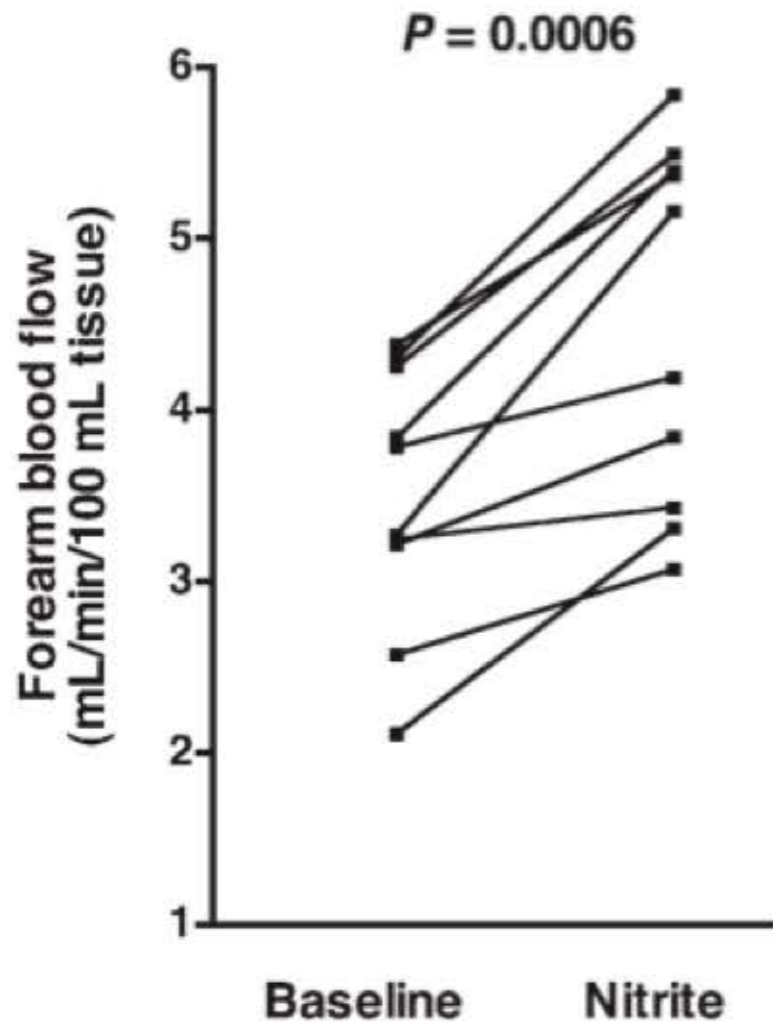
Dietary inorganic nitrate reverses features of metabolic syndrome in endothelial nitric oxide synthase-deficient mice

Mattias Carlström^{a,b}, Filip J. Larsen^a, Thomas Nyström^c, Michael Hezel^a, Sara Borniquel^a, Eddie Weitzberg^{a,1,2}, and Jon O. Lundberg^{a,1,2}

17716-17720 | PNAS | October 12, 2010 | vol. 107 | no. 41



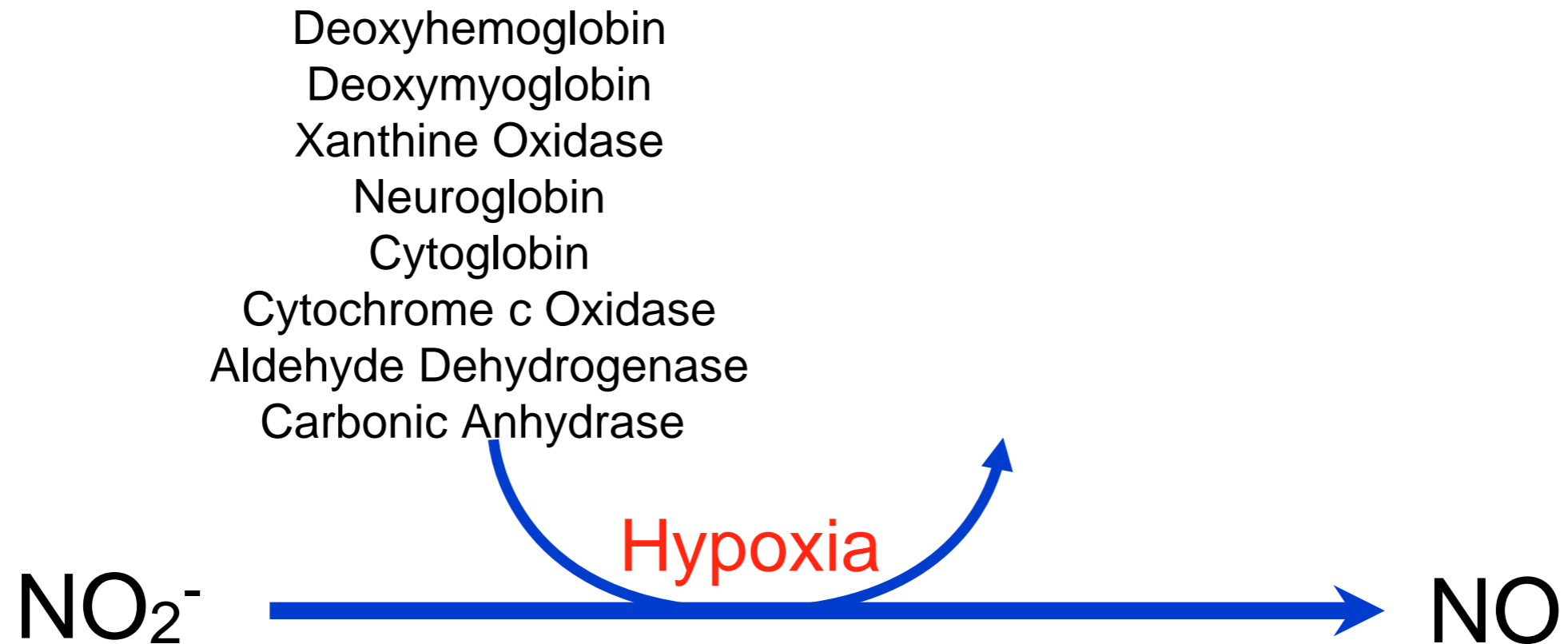
Nitrite is a vasodilator in the human forearm



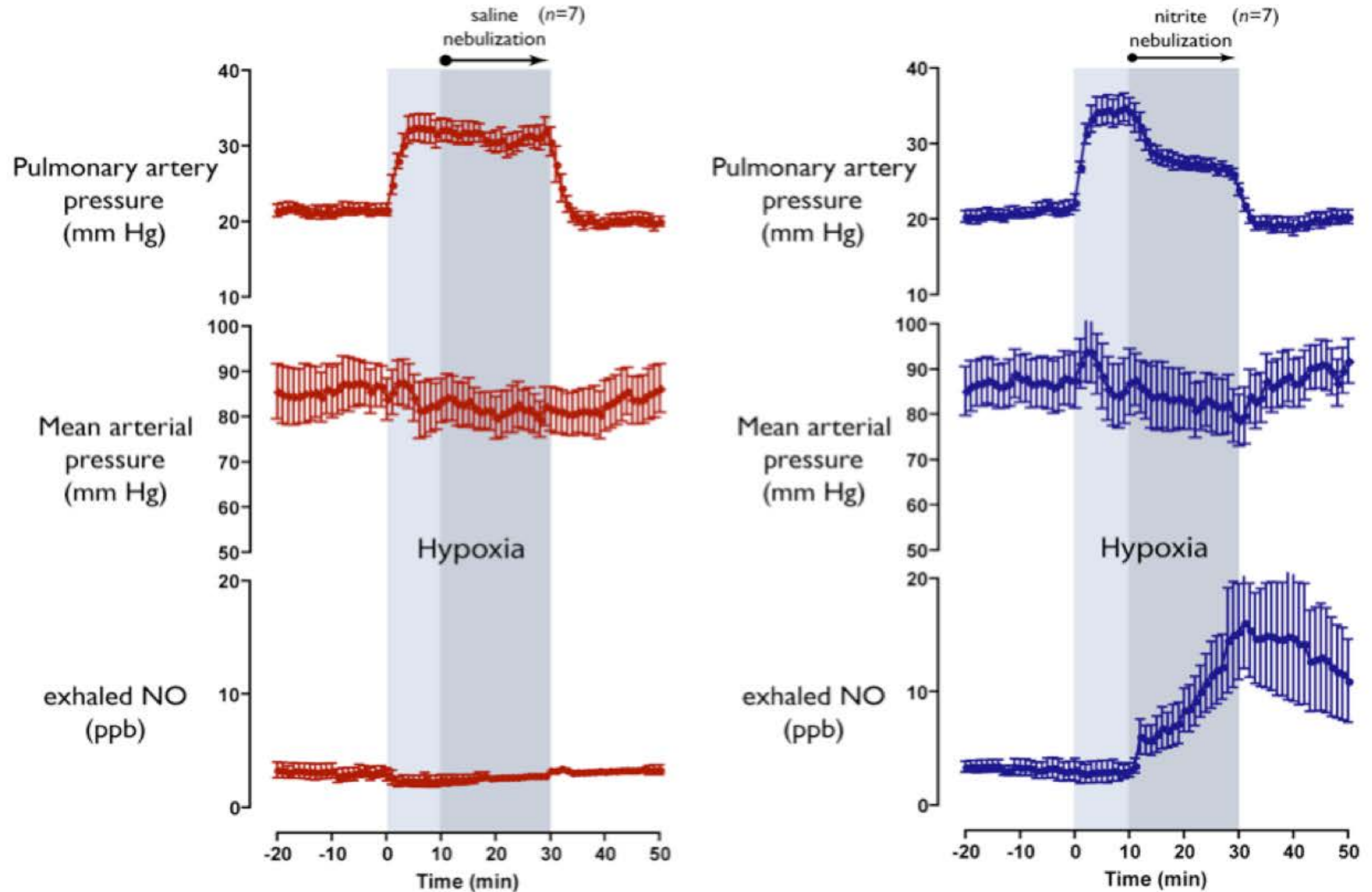
Cosby, *et al*, Nature Med. 2003 Dec 9 (12):1498-1504

Dejam *et al*, Circulation 2007;116:1821-1831

Alternative Pathways of Nitrite Reduction to NO

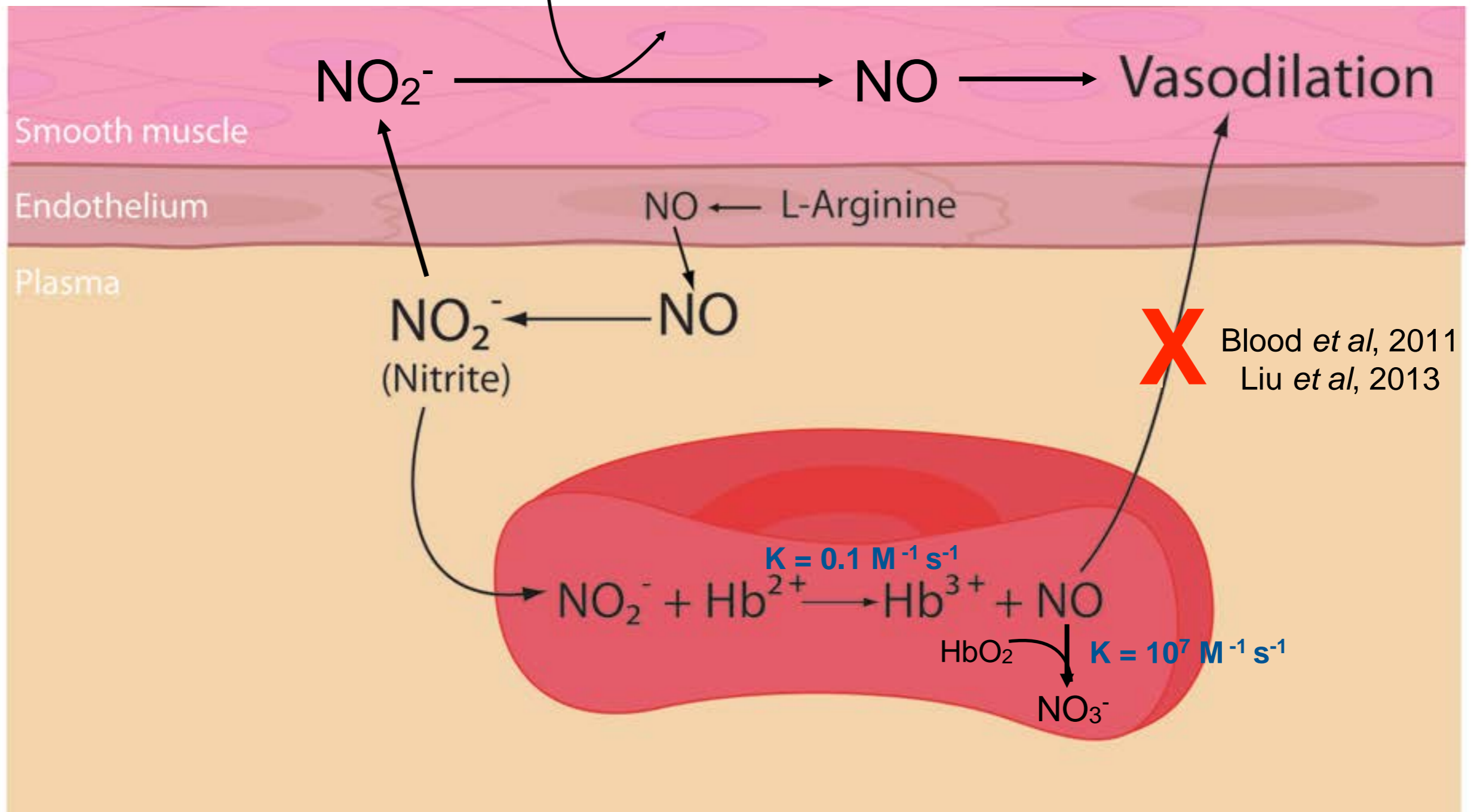


Inhaled nitrite is a pulmonary vasodilator in newborn lambs



Nitrite reduction to NO within vasculature smooth muscle?


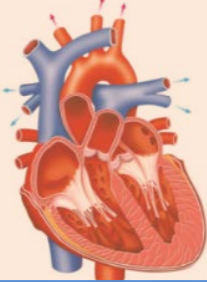

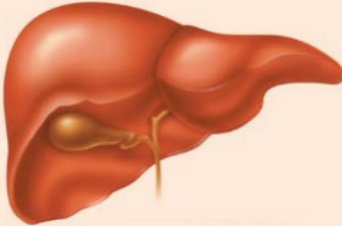


myoglobin, cytoglobin,
aldehyde dehydrogenase,
xanthine oxidase, cytochrome c



Future directions

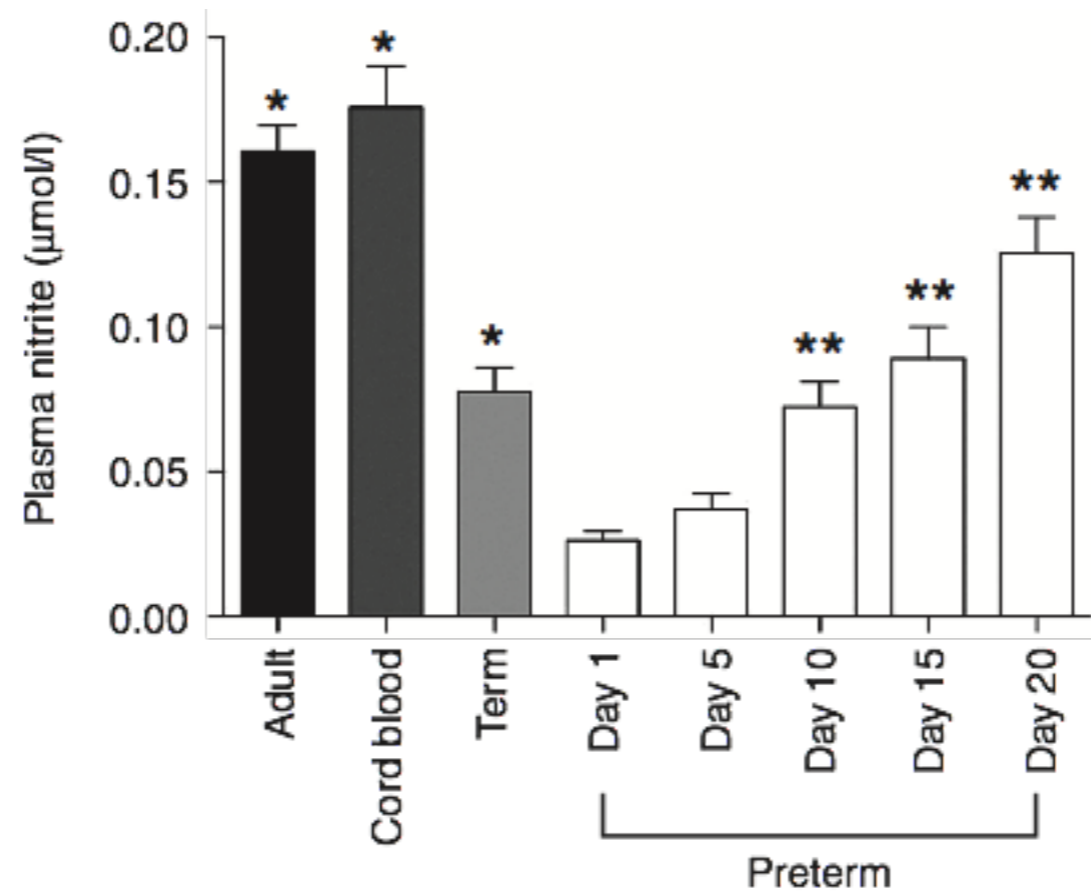
श्रीमत्पुष्पपातसाल्वधानमहासुक्तिप्रदवास्तुकाक्षयपराहृद्यजापवतावह्निरा॥६॥
याश्चैतवराहकल्पे वैवस्वतमत्तनरेऽश्रुविमतिमिकसियुगे प्रथमचरंशौवीडावतारैः
नयनेऽप्यमाशेऽशुक्लपक्षेदशम्यातिथौशोदिशीपरमृगशिरानक्षत्रैर्वैधृतियोगैश्च
नेसवितरिःमिथुनराशिगतेचन्द्रमसिःसर्वविशिष्टेपुरायदिनेऽप्युपतिप्रीतयेःकुला
सन्ननरवरेखाशिरसिपुतिविम्बितैवचन्द्रकला॥यस्यचकास्तिसेदेवःसौमोभव्याय
रिःशैलराजाधिराजःश्रीमदजेदुवर्मप्रभुचरगादयामाप्यविषोत्तमसौ॥विप्रानश्व
यर्थम्यार्णयत्तनिजकृतयजनसम्भवेसुक्तिहेतौः॥२॥आसीद्धारदाजगोत्रेहि
ःश्रीमहादेवशर्माजीवानन्दसुन्दरसिद्धिधीभूत्॥३॥तदात्मजजडधारधीरणवद
सुखापदः॥४॥उमेशचरणार्चनाधिगतकोटिविनाधिपोदिगतविलसद्यशो
गुंघ्रलक्ष्मीश्रुतास्त्राविरब्धातेद्वेधर्मपत्न्योहितस्य॥आस्तारूपीदार्यदा
॥५॥विद्यालक्ष्म्योऽश्रीकुलानन्दशर्माहीरालालपुत्रमात्मावुरूपम्॥नीत्याम
योदम्॥६॥पृथ्वीलालभैरवादिचलालभैरव्यालालचापरगुह्यल
यापूर्तेःप्रीत्यायामासदेवान्॥७॥रूपेमाधवतनूतोवितरशोवैकर्त्तनः
ताशिविर्धासिकः॥गोभीर्यसरितापतिःसुजनतानन्दैवतारापति

Nitrite Protects Against Ischemic Stress

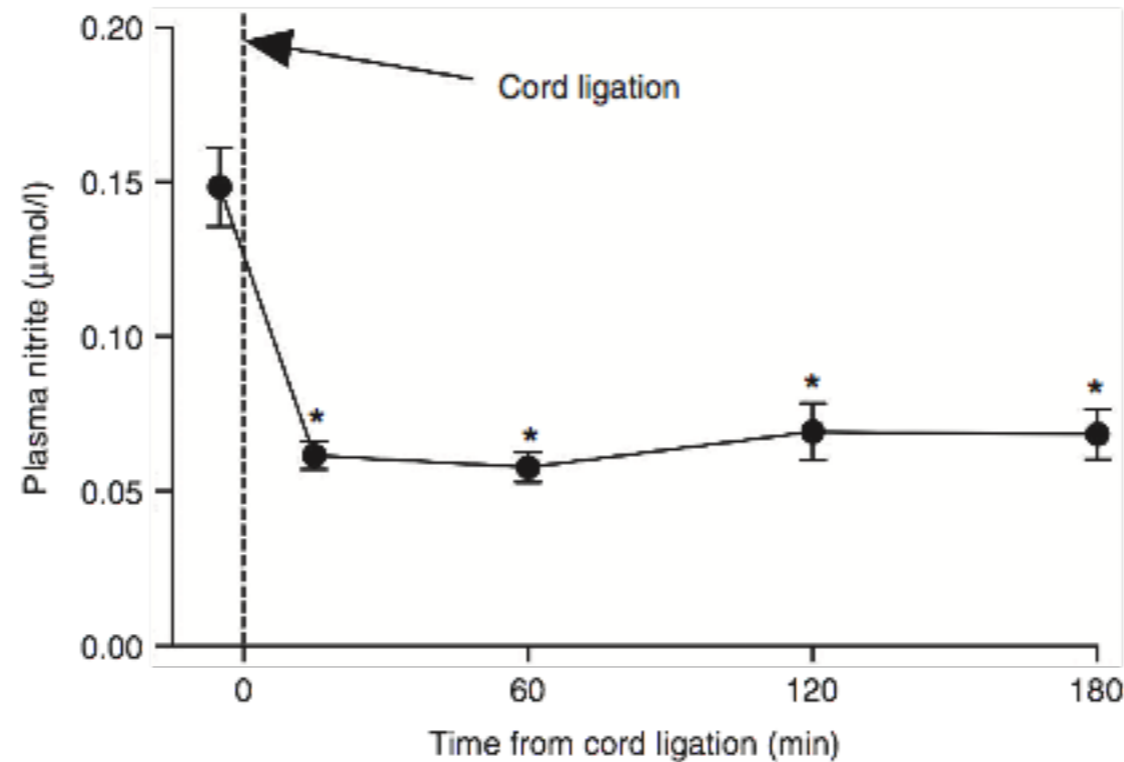
	Ischemia/Reperfusion	Rat
	Ischemia/Reperfusion Angina	Rat, Mouse, Dog
	Transplant	Rat
	Transplant Ischemia/Reperfusion	Mouse
	Ischemia/Reperfusion	Rat
	Crush Injury Ischemia/Reperfusion	Rat, Mouse, Human

Plasma nitrite falls dramatically at birth

Humans



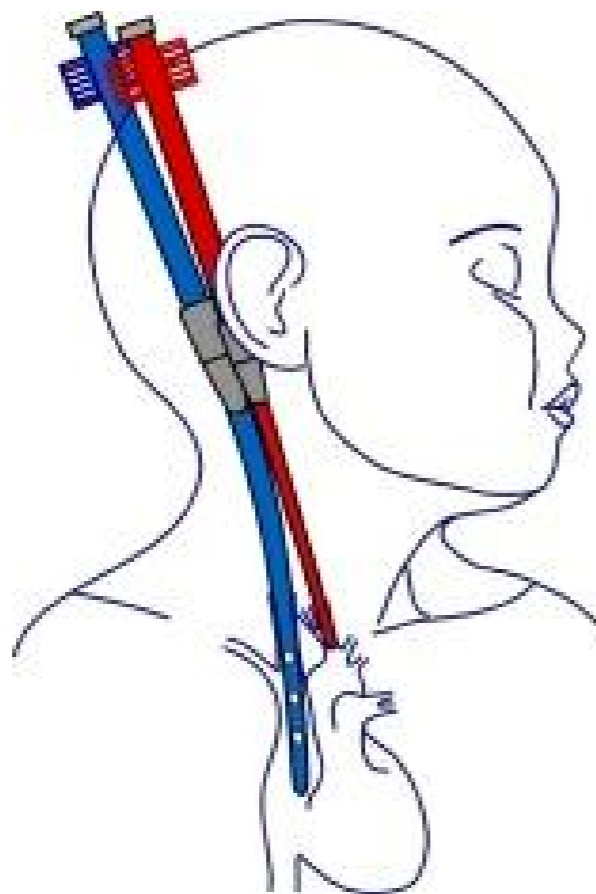
Preterm Lambs



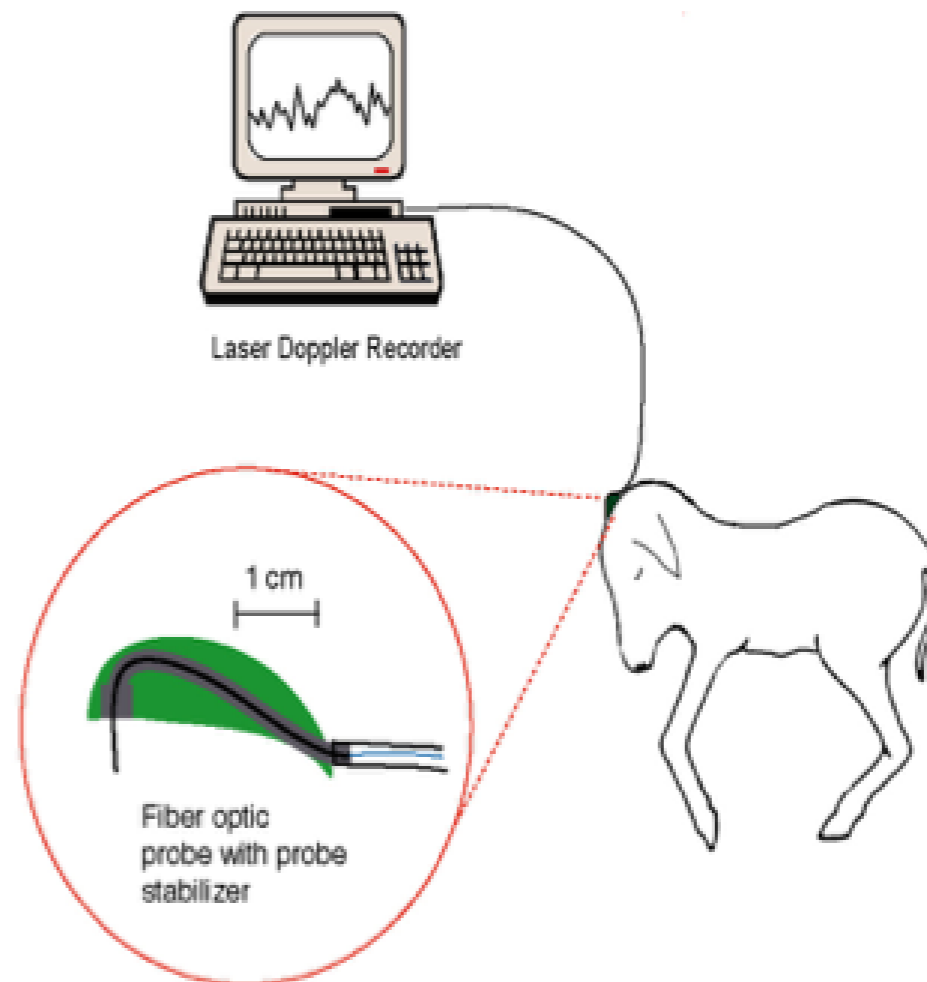
Collaborative projects

Effect of ECMO* on cerebral blood flow

Venoarterial vs Venovenous ECMO

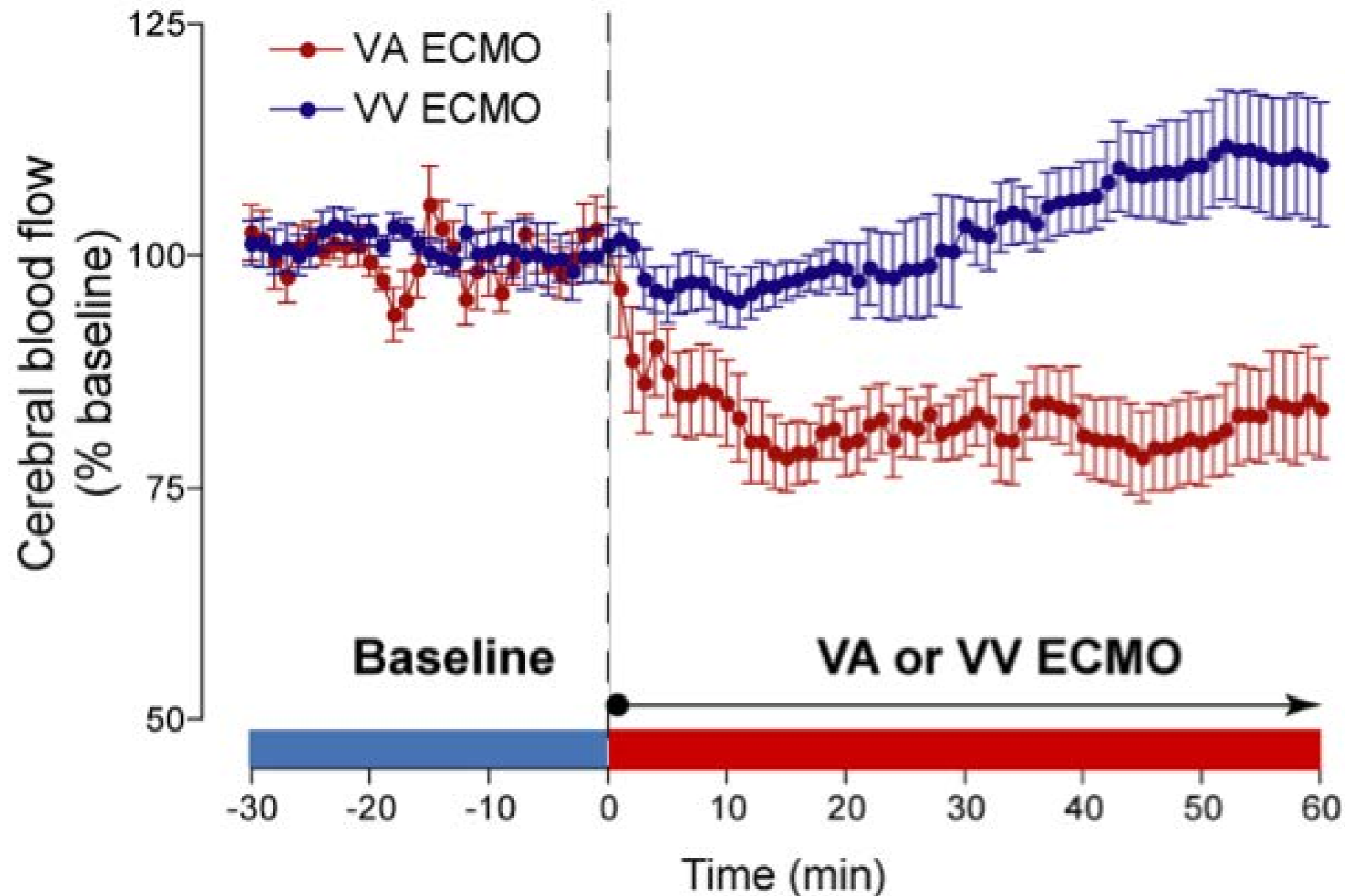


Cerebral blood flow measurement via Laser Doppler flowmetry



*Extracorporeal membrane oxygenation

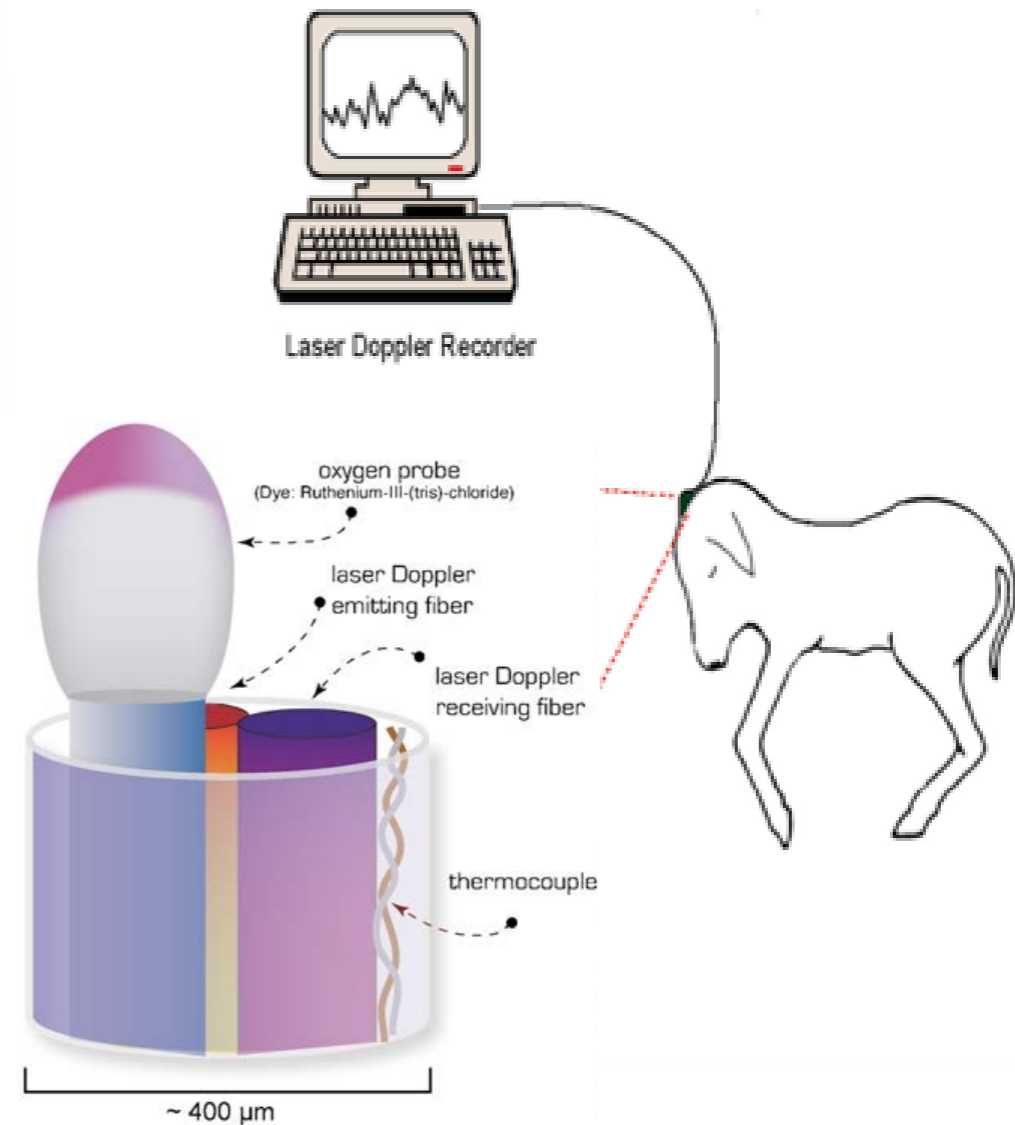
Effect of ECMO* on cerebral blood flow



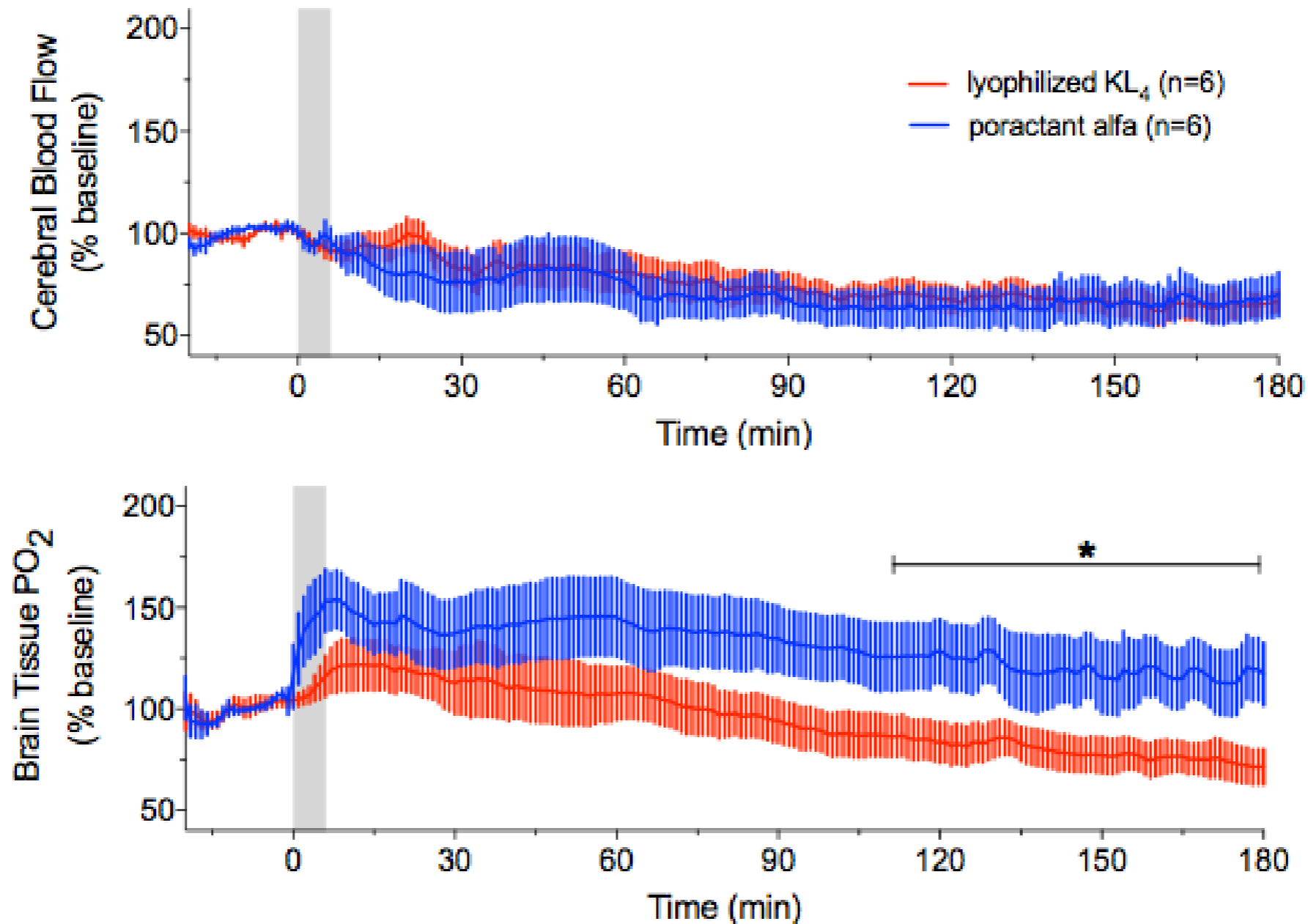
Cerebral blood flow and oxygenation during venoarterial and venovenous extracorporeal membrane oxygenation in the newborn lamb

Effect of surfactant administration on cerebral blood flow in preterm lambs

Cerebral blood flow measurement via Laser Doppler flowmetry



Effect of surfactant administration on cerebral blood flow



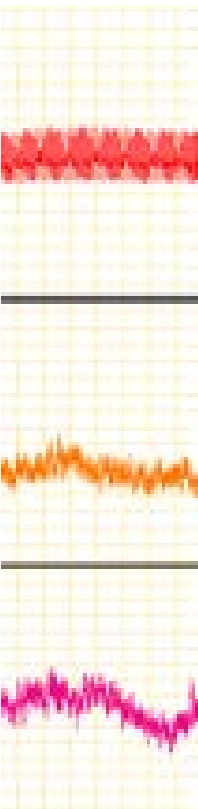
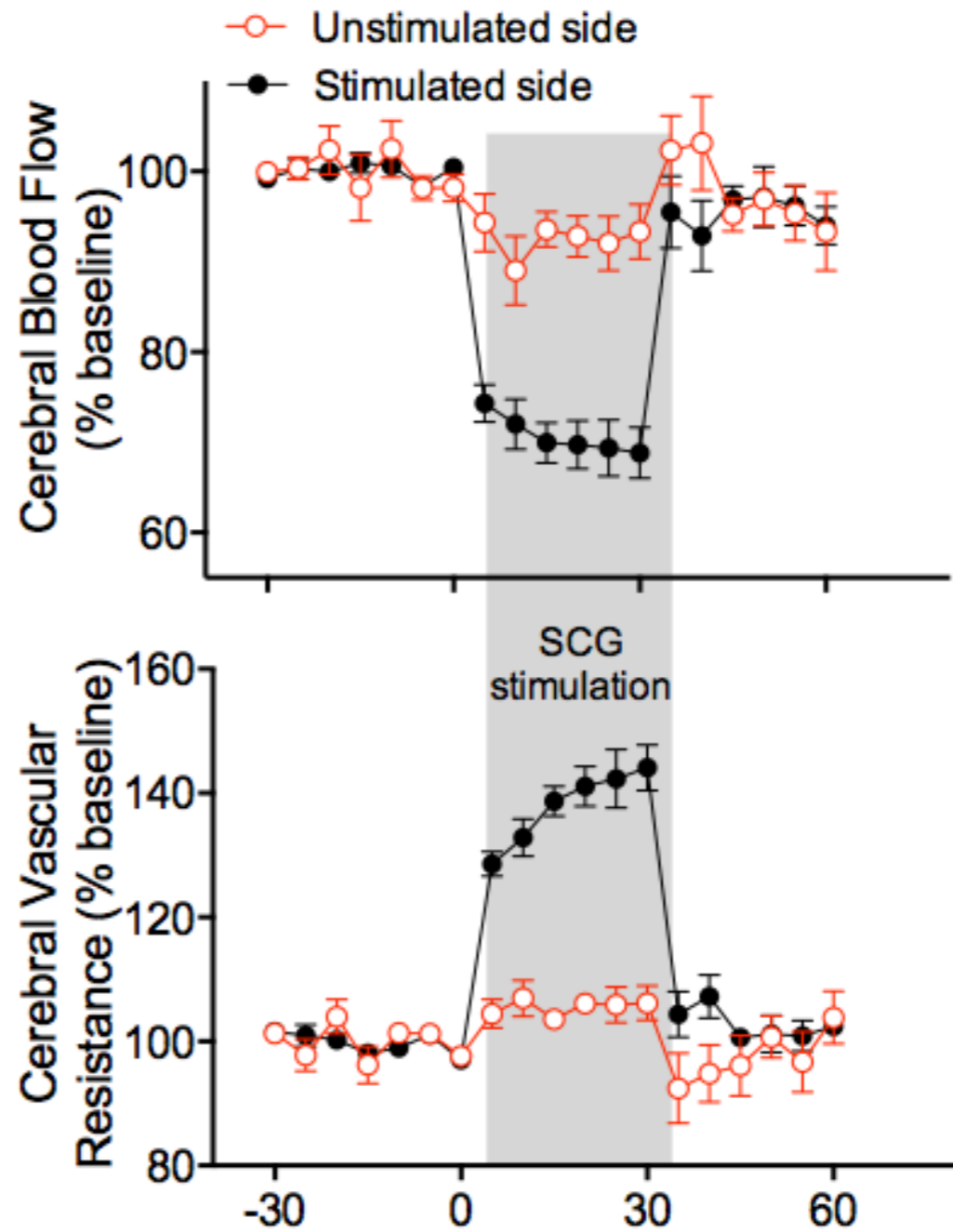
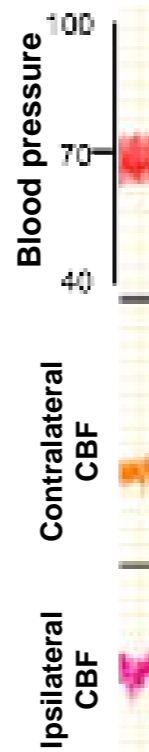
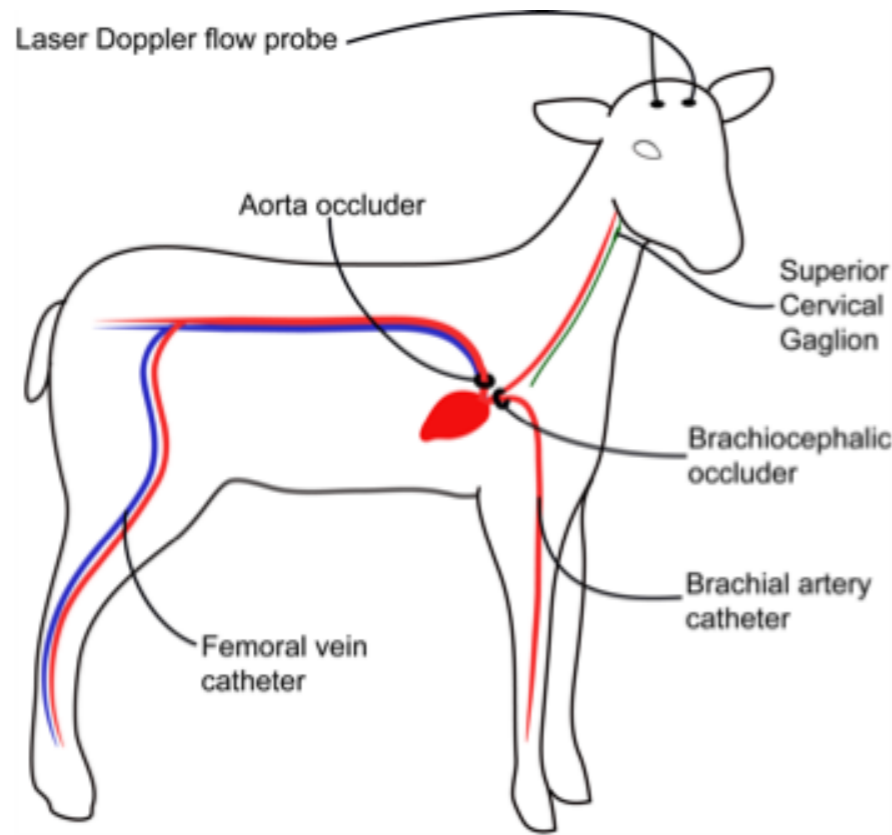
Pulmonary Distribution of Lucinactant and Poractant Alfa and Their Peridosing Hemodynamic Effects in a Preterm Lamb Model of Respiratory Distress Syndrome

MICHAEL H. TERRY, T. A. MERRITT, BENJAMIN HARDING, HOBE SCHROEDER, JEANETTE MERRILL-HENRY, JAN MAZELA, TIMOTHY J. GREGORY, ROBERT SEGAL, GORDON G. POWER, AND ARLIN B. BLOOD

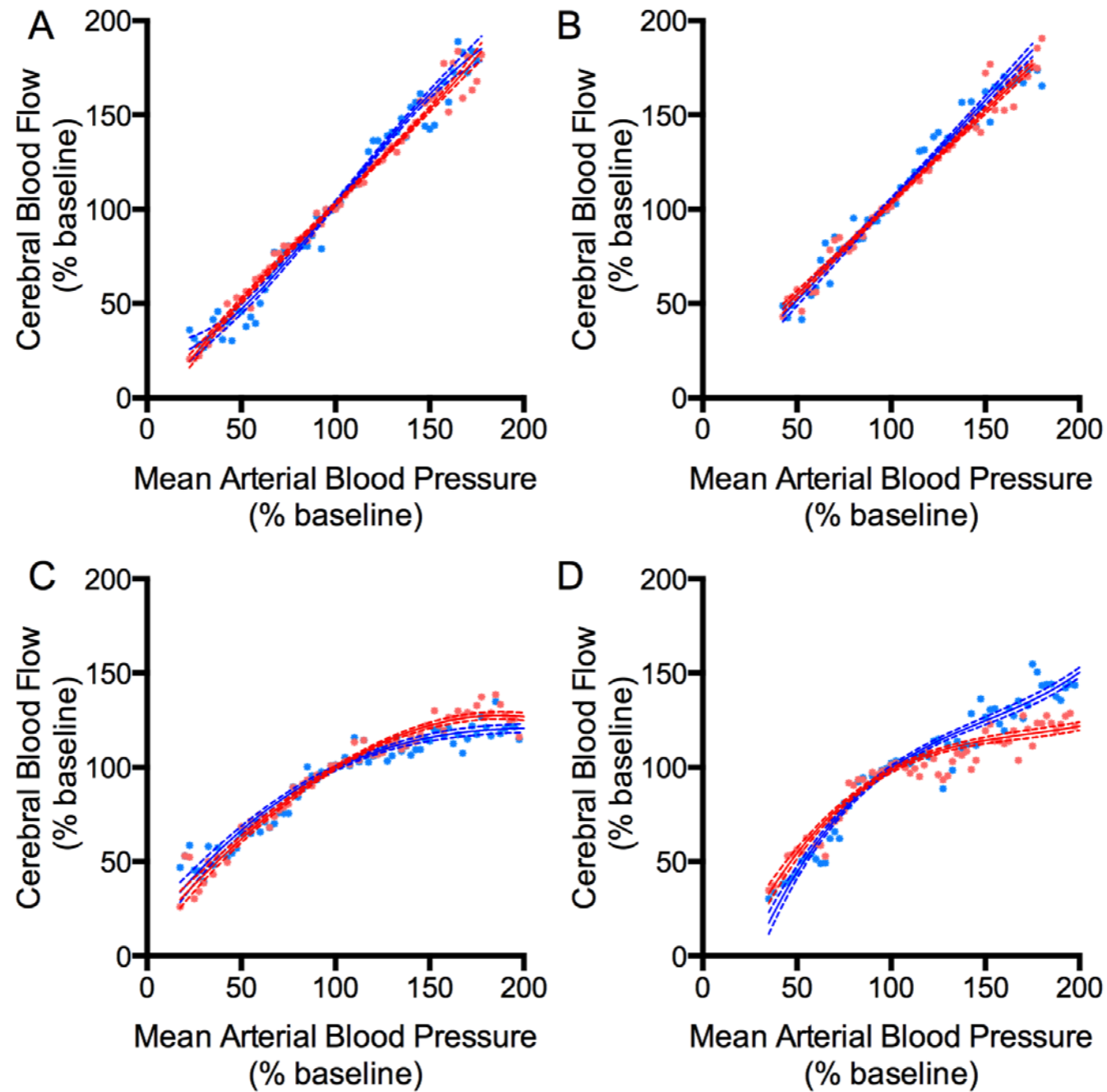
PEDIATRIC RESEARCH

Vol. 68, No. 3, 2010

Role of the superior cervical ganglion in regulation of cerebral blood flow



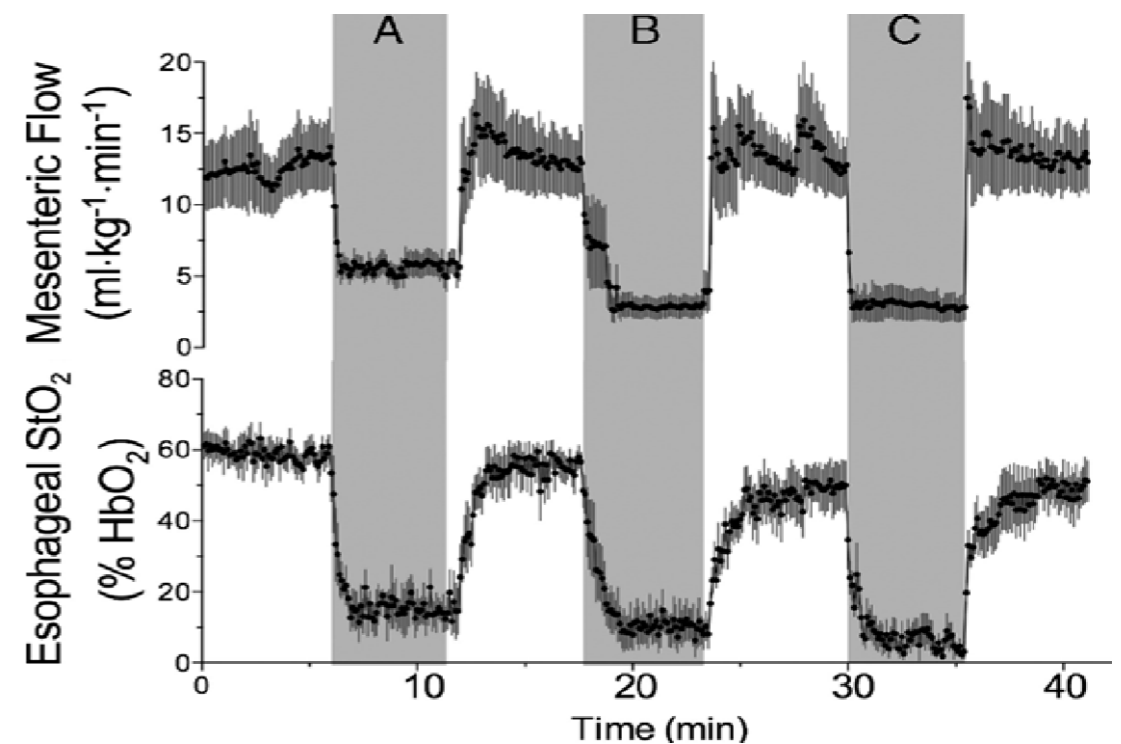
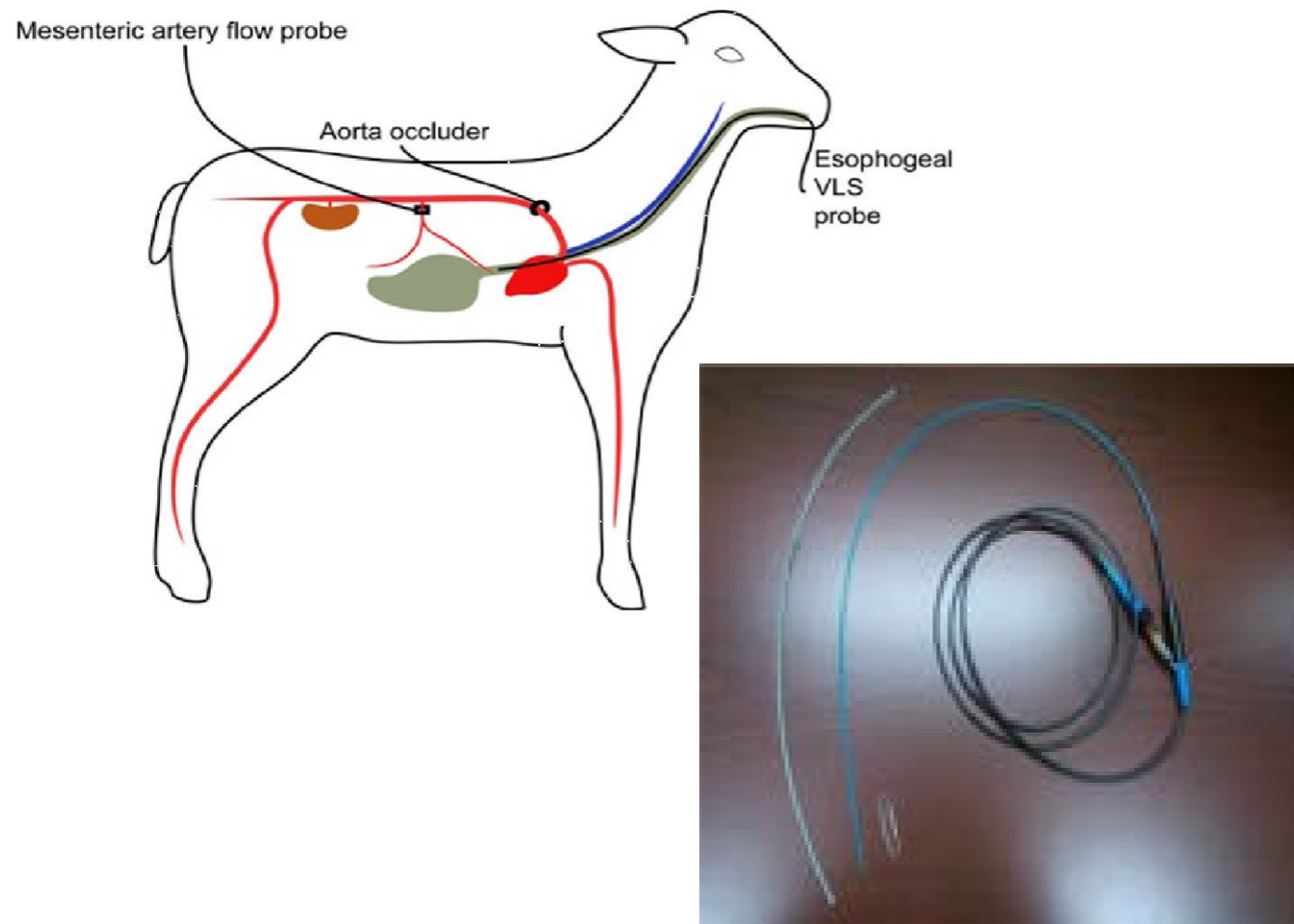
Role of the superior cervical ganglion in regulation of cerebral blood flow



Cerebral Autoregulation Is Minimally Influenced by the Superior Cervical Ganglion in Two- Week-Old Lambs, and Absent in Preterm Lambs Immediately Following Delivery

Adam J. Czynski¹, Michael H. Terry⁴, Douglas D. Deming¹, Gordon G. Power², John N. Buchholz³, Arlin B. Blood^{1,2*}

Esophageal tissue oxyhemoglobin saturation as an index of gut oxygenation



EVALUATION OF MULTIPLE MODES OF OXIMETRY MONITORING AS AN INDEX OF SPLANCHNIC BLOOD FLOW IN A NEWBORN LAMB MODEL OF HYPOXIC, ISCHEMIC, AND HEMORRHAGIC STRESS

Richard L. Applegate II,* Davinder S. Ramsingh,* Ihab Dorotta,* Chirag Sanghvi,* and Arlin B. Blood†

SHOCK, Vol. 39, No. 6, pp. 501-506, 2013

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Giang Truong

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Lawrence Longo
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Department of Pediatrics
Division of Neonatology



R01 HL095973 (ABB)



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Ivan Azarov
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