hence we do not mentioned the role of patient positioning and its impact on VAP.[1] Second, we disagree with the opinion that the orientation of the endotracheal tube below horizontal will result in reduced incidence of VAP for the reason that it is based on insufficient clinical data: three experimental animal (sheep) studies,[2–4] a randomized controlled trial with 60 ventilated infants that compared the tracheal colonization rate and not the VAP incidence in supine *versus* lateral position,[5] and unpublished observations in adult patients.

The possible body positions for orientation of the endotracheal tube below horizontal are head-down (Trendelenburg) position and lateral head-down positions. In our opinion, these positions are uncomfortable, unsafe for patients with raised intracranial pressure, and inappropriate for patients in the weaning process. Furthermore, there is evidence that the semirecumbent position is the optimal body position for VAP prevention in critically ill patients.[6]

Drs. Sathishkumar and Fassl report the advantages of the LoTrach™ tube (Hi-Lo Evac; Mallinckrodt, Athlone, Ireland) and the cuff pressure controller regarding the prevention of pulmonary aspiration during mechanical ventilation. In fact, the LoTrach tube and the cuff pressure controller are designed to offer triple protection against pulmonary aspiration: The low-volume, low-pressure cuff without folds offering effective tracheal seal at permanent tracheal wall pressure between 20 and 30 cm H2O; the triple subglottic ports for intermittent suctioning of secretions and retrograde cleansing of the entire upper airway by irrigation with normal saline; and the nonstick inner lumen designed for reduction of adhesion of biologic material and biofilm formation.

We believe that the LoTrach™ tube and the cuff pressure controller will contribute substantially to VAP prevention. However, there are still limited data about the clinical impact of the use of the LoTrach™ tube on the incidence of VAP, and further clinical research is required.[7]

Ioannis A. Pneumatikos, M.D., Ph.D., F.C.C.P.,* **Christos K. Dragoumanis, M.D., Ph.D., Demosthenes E. Bouros, M.D., Ph.D., F.C.C.P.** *University General Hospital of Alexandroupolis, Democritus University of Thrace, Medical School, Alexandroupolis, Greece. ipnevmat@med.duth.gr

References

1. Pneumatikos IA, Dragoumanis CK, Bouros DE: Ventilator-associated pneumonia or endotracheal tube-associated pneumonia? An approach to the pathogenesis and preventive strategies emphasizing the importance of endotracheal tube. ANESTHESIOLOGY 2009; 110:673–80
2. Berra L, Curto F, Li Bassi G, Laquerriere P, Baccarelli A, Kolobow T: Antibacterial-coated tracheal tubes cleaned with the Mucus Shaver: A novel method to retain long-term bactericidal activity of coated tracheal tubes. Intensive Care Med 2006; 32:888–93
3. Panigada M, Berra L, Greco G, Stylianou M, Kolobow T: Bacterial colonization of the respiratory tract following tracheal intubation-effect of gravity: An experimental study. Crit Care Med 2003; 31:729–37
4. Bassi GL, Zanella A, Cressoni M, Stylianou M, Kolobow T: Following tracheal intubation, mucus flow is reversed in the semirecumbent position: Possible role in the pathogenesis of ventilator-associated pneumonia. Crit Care Med 2008; 36:518–25
5. Aly H, Badawy M, El-Kholy A, Nabil R, Mohamed A: Randomized, controlled trial on tracheal colonization of ventilated infants: Can gravity prevent ventilator-associated pneumonia? Pediatrics 2008; 122:770–4
6. American Thoracic Society, Infectious Diseases Society of America: Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388–416
7. Young PJ, Pakeerathan S, Blunt MC, Subramanya S: A low-volume, low-pressure tracheal tube cuff reduces pulmonary aspiration. Crit Care Med 2006; 34:632–9

(Accepted for publication June 24, 2009.)

Anesthesiology 2009; 111:923–4

Wren, Boyle, and the Origins of Intravenous Injections and the Royal Society of London

To the Editor:—I read with great interest the note on Anesthesiology Reflections by Bause,[1] where he writes that in 1659 the future Sir Christopher Wren and Robert Boyle pioneered intravenous therapy, adding that by November 1660 both were meeting with 10 other scientists; gatherings that would lead to the formal chartering of the Royal Society of London for the Improvement of Natural Knowledge. I would like to comment briefly on the accuracy or precision of three aspects: The date of the pioneering intravenous injections; the credit for this invention, as the paragraph suggests coauthoring; and the origins of the Royal Society of London.

Most authors agree that the first experiments on intravenous injections took place sometime in 1656, in Boyle's quarters on High Street at Oxford, United Kingdom, and all agree in attributing to Wren the idea and execution.[2–5] Indeed, while Boyle, Wilkins, and Wren were discussing the action of poisons, the latter made the claim that he could easily contrive a way to convey any liquid poison into the mass of blood. Boyle provided a large dog, and summoned Willis and Bathurst to assist, presumably because more hands were needed to hold down the animal. Wren would later describe this in a letter, probably addressed to William Petty in Ireland, where he states that "I Have Injected Wine and Ale in a liveing Dog into the Mass of Blood by a Veine, in good Quantities, till I have made him extremely drunk, but soon after he Pisseth it out." It is perhaps interesting to add that the dog survived, grew fat, and was later stolen from his owner. Boyle himself attributed authorship to Wren when he later commented on this and other ensuing experiments of the same kind.[6,7]

As to the seminal meetings, some authors trace the Royal Society's origins back to 1645, to Gresham College in London, United Kingdom, others to Wadham at Oxford somewhat later, while still others propose a more eclectic interpretation.[8] These informal meetings, for which apparently no records were kept, were held regularly and with great enthusiasm. Remarkably, they united Royalists and Parliamentarians alike, despite the troubled times during the Civil Wars, the Commonwealth, the Protectorate, and the Restoration, when many of them lost or won their academic appointments, properties, and even liberty as a result of their allegiances. Surely, the main reason for this success is that recalled by John Wallis in 1678: "We barred all Discourses of Divinity, of State-Affairs, and the News (other than what concern'd our business of Philosophy confining ourselves to Philosophical Inquieries, and such as related unto; as Physick, Anatomy, Geometry, Astronomy, Navigation, Staticks, Mecanicks, and Natural Experiments."[9] The fact that many meetings were held or ended at a coffee house or pub must also have helped. Wren and Boyle, along with Wilkins, Willis, Wallis, Bathurst, and others, had been meeting regularly at Oxford for at least 5 yr before that gathering on November 28, 1660.

Jorge Dagnino, M.D., Pontificia Universidad Católica de Chile, Santiago, Chile. jdagnino@med.puc.cl

References

1. Bause GS: Boyle, a most skeptical chemist. ANESTHESIOLOGY 2009; 110:610
2. Anonymous: An account of the rise and attempts, of a way to conveigh liquors immediately into the mass of blood. Philos Trans R Soc London 1665–1666; 1:128–30
3. Jardine L: On a grander scale, The outstanding life of Sir Christopher Wren. New York, Harper Collins, 2002, pp 122–3
4. Tinniswood A: His invention so fertile, A life of Christopher Wren. Oxford, Oxford University Press, 2001, pp 36–7

5. Davies CSL: The youth and education of Christopher Wren. Engl Hist Rev 2008; 123:300–27
6. Bennet JA: A Study of parenthalia, with two unpublished letters of Sir Christopher Wren. Ann Sci 1973; 30:129–47
7. Bergman NA: Early intravenous anesthesia: An eyewitness account. ANESTHESIOLOGY 1990; 72:185–6
8. Frank RG Jr: John Aubrey, F.R.S., John Lydall, and science at Commonwealth Oxford. Notes Rec R Soc Lond 1973; 27:193–217
9. McKie D: The origins and foundation of the Royal Society of London. Notes Rec R Soc Lond 1960; 15:1–37

(Accepted for publication June 24, 2009.)

Anesthesiology 2009; 111:924

In Reply:—I thank Professor Jorge Dagnino, M.D., for his chronology of the founding of the Royal Society. With my six-sentence limitation on caption space for *Anesthesiology Reflections*, I thought that I had dealt reasonably with the Royal Society's nebulous origins by writing that Wren, Boyle, and others had met "by" (not "first met") in November of 1660.

Just as I acknowledged 21 yr ago, Wren was the "brains" behind the intravenous goose quill experiment of 1656.[1] So I concur with Professor Dagnino on these facts. In "Boyle, a Most Skeptical Chemist," the 1659 date in the caption was my typographical error.[2]

My thanks to Professor Dagnino for his thoughtful feedback on my telegraphic captions.

George S. Bause, M.D., M.P.H., Case Western Reserve University, Cleveland, Ohio. ujyc@aol.com

References

1. Bause GS: An historical backdrop to cardiovascular monitoring. Anesth Clin N Am 1988; 6:672
2. Bause GS: Boyle, a most skeptical chemist. ANESTHESIOLOGY 2009; 110:610

(Accepted for publication June 24, 2009.)

Anesthesiology 2009; 111:924–5

Esmolol May Abolish Volatile Anesthetic-induced Postconditioning by Scavenging Reactive Oxygen Species

To the Editor:—We read with great interest the article recently published by Lange *et al.*[1] In an *in vivo* rabbit model of myocardial ischemia–reperfusion induced by 30 min of coronary occlusion and 180 min reperfusion, the authors observed that β-adrenergic receptor blockade during early reperfusion with either the β1-adrenergic blocker esmolol or the β2-adrenergic blocker ICI 118,551 abolished desflurane-induced postconditioning cardioprotection manifested as reduced myocardial infarct size. However, neither esmolol nor ICI 118,551 had a significant effect on postischemic myocardial infract size when used alone during the first 30 min of early reperfusion, in the absence of desflurane. This is a very interesting finding. However, the more interesting point of the study, as commented on by Dr. Riess in an editorial[2] accompanying this article, is that sustained β1-blockade with esmolol during the entire period of reperfusion not only failed to abolish desflurane-induced postconditioning cardioprotection, but instead actually conferred a similar degree of cardioprotection. We want to join Dr. Riess[2] in congratulating the authors for this comprehensive study detailing the role of β-blockers in volatile anesthetic postconditioning. However, we do not entirely agree that the energy-sparing effect of β-blockade, mainly heart rate reduction, may have been the principal reason for the infarct size reduction. We propose that β-blockers may have conferred cardioprotection primarily by reducing the production of reactive oxygen species (ROS)[3,4] during reperfusion, and that esmolol may have abolished desflurane-induced postconditioning by scavenging ROS.

ROS has been shown to play an essential role in β-adrenergic signaling in cardiac myocytes.[5] Volatile anesthetic-induced generation of small amounts of ROS plays a critical role in anesthetic preconditioning,[6,7] and likely in anesthetic postconditioning as well, since they share similar mechanisms. Esmolol has been shown to increase antioxidant activity and reduce ROS-induced lipid peroxidation in patients with acute myocardial infarction.[8] Therefore, it is reasonable to postulate that esmolol abolished desflurane-induced postconditioning *via* its antioxidant action in the study of Lange *et al.*[1] If this is the case, it could be possible that the cardioprotection conferred by a combination of desflurane postconditioning and delayed β-adrenergic blockade during reperfusion could be superior to desflurane postconditioning or β-adrenergic blockade alone. We are interested in the authors' opinion on this possibility, and the clinical relevance of their findings.

It should be noted that the volatile anesthetic isoflurane-induced ROS production and anesthetic preconditioning cardioprotection is attenuated in senescent hearts,[9] likely because ROS production is already increased in the senescent. Information regarding the age or body weight of the study animal (New Zealand White rabbits) is not provided in the study of Lange *et al.*[1] Presumably, the study was conducted in young animals. It would be also interesting if the authors could provide this information and comment on the potential effect of aging on the effectiveness of anesthetic postconditioning.

Zhengyuan Xia, Ph.D., M.D.,* **Michael G. Irwin, M.D.** *The University of Hong Kong, Hong Kong, China. zyxia@hku.hk

References

1. Lange M, Redel A, Lotz C, Smul TM, Blomeyer C, Frank A, Stumpner J, Roewer N, Kehl F: Desflurane-induced postconditioning is mediated by beta-adrenergic signaling: Role of beta 1- and beta 2-adrenergic receptors, protein kinase A, and calcium/calmodulin-dependent protein kinase II. ANESTHESIOLOGY 2009; 110:516–28
2. Riess ML: The rocky road from bench to bedside: Beta-blockers and anesthetic postconditioning. ANESTHESIOLOGY 2009; 110:451–2
3. Röth E, Matos G, Guarnieri C, Papp B, Varga J: Influence of the beta-blocker therapy on neutrophil superoxide generation and platelet aggregation in experimental myocardial ischemia and reflow. Acta Physiol Hung 1995; 83:163–70
4. Röth E, Török B: Effect of the ultrashort-acting beta-blocker Brevibloc on free-radical-mediated injuries during the early reperfusion state. Basic Res Cardiol 1991; 86:422–33
5. Remondino A, Kwon SH, Communal C, Pimentel DR, Sawyer DB, Singh K, Colucci WS: Beta-adrenergic receptor-stimulated apoptosis in cardiac myocytes is mediated by reactive oxygen species/c-Jun NH2-terminal kinase-dependent activation of the mitochondrial pathway. Circ Res 2003; 92:136–8
6. Kevin LG, Novalija E, Riess ML, Camara AK, Rhodes SS, Stowe DF: Sevoflurane exposure generates superoxide but leads to decreased superoxide during ischemia and reperfusion in isolated hearts. Anesth Analg 2003; 96:949–55
7. Tanaka K, Weihrauch D, Kehl F, Ludwig LM, LaDisa JF Jr, Kersten JR, Pagel PS, Warltier DC: Mechanism of preconditioning by isoflurane in rabbits: A direct role for reactive oxygen species. ANESTHESIOLOGY 2002; 97:1485–90