Three Editorials—Three Historical Allusions

To the Editor:—I enjoyed three of the editorials in the December 2008 issue of Anesthesiology, because each one alluded to events in the history of anesthesia. In the first one I read, Orser and Saper argued that the quod pro quo for exiting the current “ether era” is tied to identifying the neural circuits and receptors responsible for the anesthetic state and designing new anesthetic drugs that are more focused in their action. 1 In the second, the effects of nitrous oxide and xenon on N-methyl-D-aspartate and α-amino-3-hydroxy-5-methyl-4-isoxazole-propionate receptors in the amygdala were compared. According to Hemmings and Mantz, the differences between the two inhaled agents “are no laughing matter”—a very nice allusion—both to the early use of nitrous oxide as a laughing gas at public demonstrations and medical student frolics in the early 1800s and to the “failed” public demonstration of nitrous oxide for surgical anesthesia by Wells, contrasted with the successful administration of ether in this setting by Morton and the subsequent declaration by the surgeon Warren, “Gentlemen—this is no humbug.” 5 Now historically primed, I read the third editorial by Davidson et al. suggesting that spinal anesthesia be used in the control group for neurotoxicity studies of general anesthetics in neonates. 4 Immediately I recalled the early 1900s argument that general spinal anesthesia, or deliberate total spinal anesthesia, even for head and neck surgery, avoided some of the problems associated with the administration of general inhalational anesthesia, such as the mortality rate attributed to chloroform and the technical problems involved with inhaling ether. 6 If we look at 50-yr snapshots, we see anesthesia for frolics in the 1800s replaced by inhalational anesthesia for surgery in the 1850s, spinal anesthesia emerging in the 1900s, a preference for general anesthesia in the 1950s, and now spinal anesthesia as the “less neurotoxic” control group. We have clearly made improvements in both approaches to anesthesia. More importantly, we have become much more rigorous and demanding in what we consider safe anesthesia.

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(Accepted for publication April 6, 2008.)

In Reply:—I thank Dr. Roy for his thoughtful integration of the three editorials. 1–5 His broad overview of the evolution of anesthetic practice highlights two important points. As a result of the hard work of our forefathers, we have developed a remarkable understanding of “what anesthetics do.” These insights have produced unprecedented advances in patient safety, primarily as a result of improved monitoring and drug delivery systems. However, we are also reminded that we still don’t understand “how anesthetics work.” This lack of knowledge has resulted in a paucity of radically new anesthetic drugs which, in turn, has contributed to a plateau in anesthesia-related mortality. 4 The specialty of anesthesiology must be ambitious and relentless in its efforts to develop safer anesthetic drugs and improved drug administration strategies. This effort will require a firm commitment to train young investigators who will bring the best science to bear on this important goal.

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(Accepted for publication April 6, 2009.)
The Aged Erythrocyte: Key Player in Cancer Progression, but Also in Infectious and Respiratory Complications of Blood Transfusion?

To the Editor:—We read with interest the study of Atzil et al.1 on the deleterious effect of storage of erythrocytes on cancer progression in two tumor rat models. Using different transfusion products, the impact of erythrocytes, leukocytes, and leukocyte-derived soluble factors on host ability to clear circulating cancer cells and host survival rates was assessed. Blood transfusion was found to be an independent risk factor for cancer progression. Surprisingly, aged erythrocytes (9 days and older), rather than leukocytes or soluble factors, mediated the effects. The authors hypothesized that aged erythrocytes may preoccupy host- innate immune effector cells, leaving tumor cells unattended.

Besides cancer progression, other adverse effects of blood transfusion may also be influenced by storage time of erythrocytes. Transfusion of nonleucoreduced aged erythrocytes was found to be associated with an increase in postoperative infectious complications.2,3 To date, the mechanism of this phenomenon is not clear. A role for leukocytes and/or soluble factors in the stored blood products has been suggested. The results of the present study may suggest another mechanism of blood transfusion-related infections. It could be hypothesized that patients transfused with aged erythrocytes may develop a disturbed host immune defense, either via suppression of the interaction of host immune cells with bacteria, or via suppression of cytokine secretion, which may result in a vulnerability to develop pneumonia or other infections. If erythrocytes indeed play a role, this may explain why studies comparing leukoreduced with nonleucoreduced red blood cell transfusions showed no effect on the incidence of infectious complications.4

Besides infectious complications, transfusion of outdated erythrocytes is associated with the onset of acute lung injury,5,7 which may be mediated by biologically active lipids and/or cytokines that accumulate during storage of blood products.5,7 In our laboratory, we performed preliminary experiments with transfusion of healthy rats with stored erythrocytes from the same animal species. Stored erythrocytes resulted in respiratory symptoms and worsening of the condition of the animals, suggestive of acute lung injury. Did the authors of the article under discussion notice any respiratory failure in the animals transfused with stored erythrocytes, as compared with controls transfused with fresh erythrocytes or saline, before the inoculation of the cancer cells?

In conclusion, the authors have pointed to aged erythrocytes as mediators of cancer progression, raising questions about potential other effects of storage of erythrocytes on host immune response. We would like to call for further experimental and clinical studies assessing the role of aged erythrocytes in transfusion-related infectious complications and on transfusion-related acute lung injury.

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Patient Blood Management and Transfusion

The very well designed animal study of Atzil et al.2 is very interesting, expressing the independent role of blood transfusion in cancer progression and, more precisely, the role of aged erythrocytes more than leukocytes. The editorial of Spahn et al.3 related to this article summarizes brilliantly the numerous disadvantages of homologous blood transfusion.

Red blood cell transfusion is a frequently performed activity in routine anesthetic practice. There are great differences between Euro-

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