proportion of drugs including anesthetics still have no infant labeling. Sufficient research to demonstrate efficacy or safety has simply not been done. Almost 200 yr after Dr. Buchan made his observations, infants are still relatively disadvantaged.

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(Accepted for publication April 6, 2009.)

Anesthesiology 2009; 111:444

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 leucoreduced 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Besides infectious complications, transfusion of outdated erythrocytes is associated with the onset of acute lung injury,[2,5] which may be mediated by biologically active lipids and/or cytokines that accumulate during storage of blood products.[6,7] 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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(Accepted for publication April 8, 2009.)

The above letter was sent to the authors of the referenced article by Atzil *et al.* The authors did not feel that a response was required.—James C, Eisenach, M.D., Editor-in-Chief.

Anesthesiology 2009; 111:444–5

Patient Blood Management and Transfusion

To the Editor:—We have read with great interest both the editorial by Spahn *et al.*[1] and the article by Atzil *et al.*[2] in the December issue of ANESTHESIOLOGY. We fully agree with the argumentation, but we want to go further into this debate.

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.*[1] 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-

The above letter was sent to the authors of the referenced article by Atzil *et al.* The authors did not feel that a response was required.—James C, Eisenach, M.D., Editor-in-Chief.