

ond, if CPB and blood transfusion affect the immune system in a similar manner, there may be no incremental adverse effect on the immune system until a sufficiently large number of packed erythrocytes have been transfused. Consistent with the notion that an adverse effect on the immune system causes reduced long-term survival (although at odds with other studies that have compared long-term results of off-pump *vs.* CPB cardiac surgery), Weightman *et al.* reported a reduced hazards ratio of 0.63 for patients who were underwent off-pump surgery where, presumably, there is less immunosuppression, although this finding (possibly because of a small sample size) was not statistically significant.

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## In Reply:

Thank you for the opportunity to respond, and warm thanks to Drs. Gross, Shander, Waters, and Roth for their interest in our study<sup>1</sup> and their valuable comments. We emphasize that we did not study the short-term effects of blood transfusion and so are not able to respond to comments relating to short-term effects. We believe that it is important not to confuse short- and long-term effects.

It is an overstatement to suggest that all doses of blood, under all circumstances, have been consistently associated with long-term harm. It is contradicted by two of the references that Gross *et al.* provided.<sup>2,3</sup> The 2002 study by Engoren *et al.* was indeed a landmark, but it showed no relationship between total 5-yr mortality and intraoperative transfusion (relative risk, 1.2; 95% CIs, 0.6–1.7,  $P = 0.53$ ). It was only postoperative transfusion or a combination of intraoperative and postoperative transfusions that had a significant association. More recently, Engoren *et al.*<sup>4</sup> have studied 993 patients undergoing cardiac valve surgery and concluded that blood transfusion was not associated with reduced long-term survival. They also studied 2,213 intensive care patients<sup>5</sup> and found that blood transfusion was associated with improved late survival. Surgenor *et al.*<sup>3</sup> studied 3,254 cardiac surgery patients; between 6 months and 5 yr after surgery “there was no association between exposure to 1 or 2 units of blood and survival” (hazard ratio, 1.06; 95% CIs, 0.91–1.24,  $P = 0.431$ ).

We make no apologies for designing our study to investigate the dose-dependent effects of allogeneic transfusion on

life expectancy. We went into the study with an open mind. We observed that the transfusion of 1–2 units of allogeneic blood products was associated with a 1.00 relative risk of death, with 95% CIs between 0.7 and 1.4. The relative risk for patients who received 3–6 units was 0.98 (0.6–1.4). We concluded that there was not a strong association between moderate transfusion of blood or blood products and long-term mortality. It would be scientifically invalid to conclude otherwise.

To consider the power limitations of our study, it may be worthwhile to estimate the effect on absolute mortality that our data allow us to exclude. We observed an absolute mortality rate of 1.8% per year; our CIs allow us to exclude a 40% increase in relative risk or a 30% decrease in relative risk. Therefore, our study allows us to estimate that a 1- to 2-unit transfusion is associated with not more than a 0.7% increase, or 0.5% decrease, in the annual mortality rate.

Neither fresh frozen plasma nor platelets are truly acellular. We included them in our count of donor exposures because both products contain leukocytes, are allogeneic, and are associated with serious acute transfusion-related immune-mediated effects. Fresh frozen plasma is implicated in the pathogenesis of transfusion-related lung injury, the most common cause of transfusion-related death in the United States.<sup>6</sup> Presumably, Gross *et al.* are not suggesting that these products can be considered free of long-term risk. Nevertheless, it is a proper scientific scepticism to question this aspect of our study design. Consequently, we have further analyzed our data, counting only red cell containing transfusions: the relative risk of long-term mortality in patients receiving 1–2 units of red cells was 0.98 (95% CIs, 0.7–1.4).

Gross *et al.* may be underestimating the importance of anemia as a predictor of long-term survival. The Atherosclerosis Risk in Communities study<sup>7</sup> of 14,410 people between 45 and 64 yr old in the general United States population showed that anemia was associated with a 1.65 relative risk of mortality. This is a considerable risk factor; it is of similar magnitude to that associated with diabetes or heart failure. This magnitude of risk has been demonstrated in many other studies. van Straten *et al.*<sup>8</sup> studied 10,025 patients undergoing coronary artery graft surgery and demonstrated a relative risk for late mortality of 1.64 in patients with mild anemia. Riva *et al.*<sup>9</sup> studied 7,536 Europeans demonstrating an association between mild anemia and late mortality of 1.86. We suggest that any study of long-term survival that does not take baseline anemia into account may be flawed. We note that some studies on the association between long-term mortality risk and blood transfusion been published without taking preoperative anemia into account. We would be interested in seeing a reanalysis of their results after this factor has been included.

We thank Gross *et al.* for recognizing an error in our results. One hundred seventy-three patients, not 183, died who had been transfused and who did not have a history of cancer. This typographical error was the authors' responsibility not the publisher. Nevertheless, the preponderance of cancer-related deaths in the nontransfused group remains

unlikely to have occurred by chance. We note this simply as an observation; diagnoses recorded on death certificates were never part of our original hypothesis and cannot be used in the inferential process. We do not agree with Gross *et al.* that it is scientifically valid to include a long-term outcome (death with a cancer-related diagnosis) in a predictive model based on the perioperative physical status of the patient.

Dr. Roth's suggestion that blood transfusion and extracorporeal circulation may have synergistic adverse effects is not unreasonable. Certainly, this is one explanation for the observation that cardiac surgery is the only clinical setting where adverse transfusion-related immunomodulation effects have been conclusively demonstrated.<sup>10</sup> Our study data does not help to clarify this suggestion, however, as most of our transfused patients were exposed to extracorporeal circulation.

None of this is any reason to promote the use of blood. The short-term risks are compelling, as are the huge costs and the ever diminishing resource. However, we should not be misinforming patients who have survived more than 2 months after coronary artery grafts that they have a serious risk of premature death as a result of a moderate transfusion of blood products.

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## Exposure Limits to Magnetic Resonance Imaging Fields: Invisible Land Mines or Fields to Mine

### To the Editor:

We read with interest the article by Roh *et al.* concerning exposure to low-frequency electromagnetic fields (EMFs) and wish to comment on another great source of exposure to EMF that anesthesiologists face in the hospital. Although the risk factors of magnetic fields are well known for patients, exposure limits to EMFs are unknown in healthcare providers who are continuously exposed to the magnetic resonance imaging (MRI) environment.<sup>1,2\*</sup> The MRI environment exposes anesthesiologists to static and gradient magnetic fields, with the exposure limits dependant not only on the strength of the MRI scanner (1.5 T *vs.* 3.0 T) and length of the scanning sequences but also on which anesthetic technique is chosen and whether the intravenous pumps, monitors, and anesthesia machines used are MRI compatible.

The lack of MRI safe or compatible monitors and machines forces the anesthesiologist to choose a technique that requires being in the magnet room closer to the magnet bore, and thus potential exposure to higher levels of EMF. Not only the exposure is potentially greater but also the tracking of individual anesthesiologist's exposure time during monitoring is lacking.

Because of the lack of studies of healthcare personnel to the long-term risks of EMF, certain groups are beginning to examine issues such as risk of mortality or cancer rates in personnel working in the MRI environment. Numerous groups, including the World Health Organization, National Health Service (United Kingdom), and the Health Protection Agency, are becoming involved in the design and epidemiologic studies about long-term exposure to EMF in healthcare personnel working in MRI are implemented. The European Union is also proposing a directive that will limit the exposure of healthcare workers to the EMF of MRI magnet rooms. Implementation of these directives will ban anes-

Timothy J. Brennan, Ph.D., M.D., served as Handling Editor for this exchange.

\* Keevil S. The EU physical agents (electromagnetic fields) directive and its impact on magnetic resonance imaging. Available at: <http://www.ipem.ac.uk/docimages/1581.pdf>. Accessed September 3, 2009.