variant of the known congenital biochemical abnormalities involving these vitamins, such as hyperhomocystinemia.

Nitrous-oxide–induced increases in plasma homocysteine have been correlated positively with altered endothelial function.[4] Increased plasma homocysteine concentration have strong association with increased inflammation.[5,6] Increased homocysteine concentrations are strongly correlated with the microvascular complications of diabetes, including neuropathy.[7] The ENIGMA trail suggested that if nitrous oxide is used for more than 2 h in patients, it increases their long-term myocardial infarction risk.[8] Hyperhomocystinemia is also well described as a factor for central retinal artery occlusion and central retinal vein occlusion.[9–11] This is precisely what the injury in perioperative visual loss seems to be.

If this speculated link between nitrous oxide use and perioperative vision loss should ever find any more supporting scientific evidence, it could suggest utility of simple protective strategies to avoid both postoperative visual loss and inflammatory peripheral neuropathy. One remedy could be to administer folate and vitamins B6 and B12 as premedication to patients before they undergo long duration surgery, especially spinal surgery, when using nitrous oxide in the anesthetic. In one preoperative study of 390 patients scheduled for major surgery, 0.2% individuals had a preexisting folate deficiency and 7.5% individuals had preexisting increased plasma homocysteine concentrations.[12] Those individuals could possibly be a higher risk for blindness or postoperative inflammatory neuropathy than are the other patients. The authors proposed administering routine preanesthetic folate and vitamin supplements when nitrous oxide was planned to be used on patients undergoing major surgery. The alternative protective remedy would be to avoid use of nitrous oxide surgeries that present the risk of vision loss.

Nitrous oxide is not devoid of benefits and has been shown to reduce long-term pain, possibly *via* its *N*-methyl-D-aspartic acid receptor blocking effects.[13] Thus, the overall place of nitrous oxide use in anesthesia remains a matter of debate.

It is likely that multiple risk factors for visual loss after long duration spinal surgery will remain, and all have a complex interplay with no single remedy being able to eliminate the risk of blindness.

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(Accepted for publication April 26, 2012.)

It's Still the Water

To the Editor:

After publication of the first report by the American Society of Anesthesiologists Visual Loss Registry Study Group,[1] I submitted a Letter to the Editor in which I stated that administration of excessive volumes of crystalloid fluid may be the cause of ischemic optic neuropathy (ION) and recommended that crystalloid fluid therapy not exceed 40 ml/kg, regardless of the duration of the posterior spinal surgery.[2] In reply, Dr. Warner stated that my recommendation was dogmatic and unsubstantiated, which was true, but he also did not provide any documentation that it was invalid. Now we have additional evidence that my recommendation regarding crystalloid fluid therapy was on target.

In their recent report, the Visual Loss Study Group did a retrospective comparison of a number of variables in their database of 80 patients with ION with those from 315 carefully selected, matched control subjects who underwent posterior spinal surgery but did not experience ION.[3] The Study Group identified a number of highly significant differences ($P = 0.001$) between the ION and control subjects. Three significant differences that are interrelated stand out. The

total volume of fluid replacement and the total nonblood fluid replacement were greater in the ION patients, and the administration of colloid as a percentage of the total nonblood replacement was less in the ION patients. The only remaining fluid in this analysis would be crystalloid. These findings directly support the concept that the crystalloid fluid volume was significantly greater in the ION patients, although a direct comparison of the volume of crystalloid administered in the two groups did not reach significance.

Other significant differences between the two groups included gender, obesity, use of the Wilson frame, duration of anesthesia, and estimated blood loss. Both the Study Group and Dr. Warner in his editorial[4] suggested that ION may be less common in women than men because of the protective effect of estrogen. A simpler and more reasonable explanation for the difference is that most anesthesia providers are more likely to give larger volumes of crystalloid fluid to men weighing 80–120 kg than they are to women weighing 60–80 kg. With respect to obesity, the Study Group suggested that positioning the obese patient prone may increase intraabdominal, intrathoracic, intraocular, and venous pressures and produce ischemia of the optic nerve by a variety of mechanisms. Another more plausible explanation would be that if prone positioning did increase venous pressure in the obese patients, it would be manifest most profoundly as blood loss at the operative site, which in turn, would necessitate greater fluid administration, including crystalloid fluid. Finally, the Study Group suggested that the reason that ION was more common with use of the Wilson frame was because the head is more dependent with its use. However, this explanation is only conjecture because the exact positioning of the head was not documented in all of the patients who experienced ION while on the Wilson frame. When using the Wilson frame, the head need not be dependent because it can be supported in the neutral position with pillows and head supports, and this may have been done in some of the ION patients on the Wilson frame. I do not believe that exactness in head position is necessary provided crystalloid fluid volume administration is limited. We do a large number of robotic-guided, laparoscopic, retropubic radical prostatectomies with the patients in a very steep Trendelenburg position for 4–6 h. The crystalloid fluid volume is limited to less than 1 l until the patient is returned to the level position to avoid fluid collection in the bladder, which will obscure the operative field when the bladder is opened. We have not had a case of ION in this population. Two things stand out in the reported cases of ION occurring after prostate surgery: the patients were in a Trendelenburg position for 4–6 h, and they received approximately 5–10 l crystalloid fluid.

The recent report of the American Society of Anesthesiologists Task Force on Perioperative Visual Loss[5] advocates the use of both colloid and crystalloid fluids but does not recommend any limit on the latter. Based on the evidence to date, which admittedly is mostly circumstantial, I would urge anesthesia providers to strongly consider limiting crystalloid fluid therapy to less than 40 ml/kg regardless of operative length. With this change alone, I believe that we will experience a measurable decrease in the incidence of ION.

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(Accepted for publication April 26, 2012.)

In Reply:

We would like to thank Drs. Kempen, Raw, and Larson for their interest in our study on determining risk factors for perioperative ischemic optic neuropathy (ION) after spinal fusion surgery in the prone position.[1] Dr. Kempen's suggestion to perform spine surgery in the lateral position, instead of the prone position, is intriguing. We have also considered this possibility in the past and queried our surgical colleagues. In special situations, such as second or third trimester pregnancy, when postponement of surgery is not feasible, spine surgery has been performed in the lateral position. However, the "up-down" manipulations required in the lateral position are technically more difficult than the more symmetric "right-left" manipulations in the prone position. Achieving ideal spinal alignment is much more challenging technically in the lateral position. Many surgeons rely on the lordosis imparted by some of the spinal frames in the prone position to provide optimal "anatomic" alignment for fusion.

We agree with Dr. Kempen that further study should be performed to examine the relative risks and benefits of staging very prolonged spine surgery with expected high blood loss, as we noted on pages 22 and 23 of our article.[1] The supposition that this injury may reflect the coincidental occurrence of spontaneously occurring ION in a general non-