

## Response to Rossaint and Colleagues

**Daniel I. Sessler**

*Department of Outcomes Research Anesthesiology Institute, Cleveland Clinic, Cleveland, USA*

**R**ossaint and colleagues make some remarkable assertions that are simply unsupported by available evidence.

**Assertion:** Nitrous oxide is associated with a high incidence of nausea and vomiting. **Facts:** IMPACT was a randomized trial of nitrous oxide versus nitrogen in more than 5,000 patients. The results clearly demonstrate that nitrous oxide causes half as much nausea and vomiting as volatile anesthetics (1).

**Assertion:** Nitrous oxide promotes infection. **Facts:** ENIGMA-2, a randomized trial of more than 7,000 patients, clearly shows that the drug does not augment infection risk (2).

**Assertion:** Nitrous oxide damages the heart and brain. **Facts:** ENIGMA-2, the largest and most recent trial of nitrous oxide, clearly shows that the drug does not increase the incidence of cardiovascular events (2). There is not a shred of evidence to support Rossaint's unreferenced assertion that nitrous oxide damages the brain.

**Assertion:** Nitrous oxide is toxic. **Facts:** There is no question that nitrous oxide has biochemical effects—just like every drug. That there are regulatory guidelines for *chronic* exposure is not evidence of clinical toxicity in anesthetic use. In fact, there is no convincing evidence that chronic exposure is dangerous. The guidelines are largely based on one marginal study which purported to show an increase in spontaneous abortion amongst dental assistants chronically exposed to nitrous oxide in unscavenged environments (3). That weak epidemiologic analysis would not be taken seriously today. There is not the slightest evidence of clinical toxicity related to anesthetic use.

Rossaint and colleagues also make a number of essentially irrelevant observations, for example that pipeline errors have harmed patients—the last being about a decade ago. Given universal inspired gas monitoring, it is hard to believe that there will be more such events in modern hospitals. It certainly isn't a convincing reason to avoid nitrous oxide. The greenhouse effects of anesthetic use of nitrous oxide are trivial (most nitrous oxide is released from soil by entirely natural processes). Concern about the environment is appropriate, but people should focus on interventions that make real differences—and nitrous oxide is not among them.

In summary, nitrous remains a useful anesthetic adjuvant. Aside from a small amount of nausea and vomiting (much less than from volatile anesthetics), the drug does not cause serious complications. A very large randomized trial, ENIGMA-2, clearly demonstrates that the drug is safe. It is obviously possible to provide perfectly adequate anesthesia without nitrous oxide, but clinicians should not avoid the drug for fear of toxicity.

**Address for Correspondence:**

Daniel I. Sessler

E-mail: DS@OR.org

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