We agree with Weiniger's statement that increased sensitization to latex in pregnant patients could be a potential danger in the labor and delivery suite. Conversion to a latex-free hospital environment could be possible, but in our opinion additional investigations in larger groups of patients are needed to better define this potential high risk.

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Is a Weekend Too Long?

To the Editor:

I read with interest (and concern for those gestating) the article by Palanisamy *et al.* analyzing adult Sprague-Dawley rats exposed to isoflurane *in utero*.[1] This was clearly a well-done study demonstrating reduced spatial memory and reduced anxiety in those animals exposed to isoflurane *in utero* during a time of critical brain development. The question arises as to how this may apply clinically to humans. The gestational length described in this study was 22 days, or 528 h. The study exposed subjects to 4 h of isoflurane. Therefore, the intrauterine exposure to isoflurane accounted for 0.758% of the total gestational period. This seems miniscule, but when placed in perspective, is a significantly long period of time. In humans, a term gestation is 40 weeks, or 6,720 h, meaning a similar exposure in pregnant women would total 50 h, 55 min, and 48 s. It should not be surprising that exposing the developing fetal brain to isoflurane for more than 2 days might cause a reduction in spatial memory. After all, the effect of isoflurane on plastic water traps is well described.[2,3] Although the effect of volatile anesthetics on the developing brain is a fascinating and important topic, further study should include exposures that are clinically relevant to the human developing brain. In the meantime, it can be recommended that we avoid general anesthesia in pregnant women undergoing operations lasting longer than 50 h.

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In Reply:

We appreciate the fact that Dr. Shear took an interest in our recent study showing spatial memory impairment in the adult male offspring of pregnant rats exposed to isoflurane.[1] His analogy that the brain is like a water trap is silly, and the argument that 4 h of anesthesia during rat gestation is equivalent to a weekend of anesthesia in humans, and therefore not clinically relevant, is mathematically correct but scientifically simplistic. The rat brain and human brain are obviously different. In comparison with that of the rat, for example, the human brain has approximately 430-fold more neurons, a more intricate dendritic arbor, and a markedly larger and more complicated cortical surface (accounting for 77% of brain volume *vs.* just 30% in the rat).[2,3] Of particular relevance for gestational exposure to anesthetics, the human brain has more neural stem cells, which have threefold more mitotic cycles and must traverse far longer distances to reach the right place at the right time than those in the rat. In addition, there is the fact that the human brain does far more complicated things (such as math), which requires more precise and complex connections and circuits. In short, the human brain is exponentially more intricate than the rodent brain. This is why we were careful not to extrapolate our results in the rodent to humans. More to the point, however, to the extent vulnerability is proportional to complexity (see recent events on Wall Street), it is quite plausible that the developing human brain is actually more easily damaged by general anesthetics than the rodent brain or, alternatively, that the consequences of injury are more noticeable because the demands on the system are greater in humans. Humans,

for instance, are more sensitive to perinatal asphyxia-induced neuronal injury than rats.[4] Moreover, we know from recent studies in neonatal monkeys, a species phylogenetically closer to humans than rats, that it does not take a weekend of anesthesia to induce a 13-fold increase in neuronal degeneration—5 h of isoflurane will do it.[5] The answer to whether general anesthetics harm the developing human central nervous system will come only from research, not simple math that fails to take into account the myriad differences between the rodent and human brain. In the meantime, we recommend focusing scientific debate on how general anesthetics may affect "plasticity" of the human brain rather than the plastic in water traps.

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