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Cimetidine—Unresolved Issues

*To the Editor:*—The recent editorial by Moir<sup>1</sup> states that "there is now justification for replacement of oral antacid by cimetidine before elective cesarean section." Furthermore, in the original paper, Hodgkinson *et al.*<sup>2</sup> confirm that cimetidine crosses the human placenta in large amounts.<sup>3</sup> Both of these points must be addressed.

First, cimetidine has not been recommended by the FDA for use in pregnant or nursing women or children under 16 years of age. Are we justified from a medicolegal viewpoint in using this drug if no added benefit has been clearly documented?

Second, although Apgar and neurobehavioral scores are apparently unaffected,<sup>2</sup> potential long-term side-effects have not been ruled out. A report by Glade *et al.*<sup>4</sup> described a transient rise in liver enzymes in a newborn exposed to cimetidine before birth. Furthermore, as demonstrated by Goetzman and Milstein,<sup>5</sup> tolazoline, a dilator of pulmonary vasculature, acts as an H<sub>2</sub>-receptor agonist in the lung. It is yet to be determined whether cimetidine, by way of its action at the H<sub>2</sub> receptor, contributes to increased pulmonary vascular resistance in the newborn.

We believe that both of these questions must be re-

solved before cimetidine is introduced into routine use in obstetrics.

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*In reply:*—Drs. Berman and Patel raise some important points in their letter and I am grateful for the opportunity to answer them.

There is no doubt that cimetidine crosses the placenta in substantial amounts but that Apgar and neurobehavioral scores apparently are unaffected. The apparent safety of cimetidine and the allied agent ranitidine has now been confirmed in several thousand cases in the United Kingdom when given during labor or before elec-

tive cesarean section. The question now raised is whether and in what circumstances cimetidine administered to the mother causes a transient rise in neonatal hepatic enzymes. In the case reported by Glade *et al.* and referred to by Berman and Patel the infant weighed only 1,676 g when delivered by the breech at 37 weeks gestation, subsequently developed jaundice and hepatomegaly, but was clinically well when 60 days of age. The mother had received 1,200 mg cimetidine daily for one month before