

delivery as treatment for a peptic ulcer. This grand total of 36,000 mg cimetidine is probably not relevant to the administration of a single dose of 300 mg before an elective cesarean section. If this attitude is not accepted, then ranitidine may be substituted for cimetidine on the grounds that the former agent is said not to affect hepatic enzymes. For this reason, but mainly because of a longer action, ranitidine is now used in this hospital before elective section.

Working in the United Kingdom I do not feel competent to comment on the statement that the F.D.A. does not recommend cimetidine for use in pregnant women. While this may be a justifiable view concerning longer term therapy for peptic ulcer, it may be inapplicable to the administration of one or two doses before delivery.

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Narcotic Analgesia—Ceiling Effect?

To the Editor:—The issue of a ceiling effect of respiratory depression due to narcotic agonist/antagonist drugs has become important in the consideration of the new narcotics. The question of a ceiling effect of the analgesia from narcotics is perhaps more important and recently has been brought to the attention of your readers in two articles by Murphy and Hug.^{1,2} These authors have found that fentanyl as well as morphine, butorphenol, and nalbuphine reduce the MAC requirement for enflurane in the dog a maximum of 67% regardless of the dose of narcotic. Additional studies by DiFazio and co-workers in rats anesthetized with cyclopropane is in agreement.^{3,4} We also demonstrated a similar analgesic ceiling effect of meperidine on the MAC for halothane in dogs.⁵ In our study, we used three intramuscular doses of meperidine: 2.75, 5.5, and 11.0 mg/kg and observed no significant difference in reduction of MAC between the 5.5 and 11.0 mg/kg dose (66 and 70%, respectively).

Thus, a ceiling effect of meperidine was reached when halothane MAC decreased approximately 68%, strikingly similar to the maximum reported by Murphy and Hug in the reduction of enflurane MAC with different narcotics. If there is a ceiling effect of analgesia produced by narcotics in humans, it is extremely important to know since we are seeing many narcotic studies and narcotic promoters who would convince practitioners that the more narcotic administered the more analgesia is produced. Indeed, there may be a species difference between dogs and humans. Also, there may be acute tolerance to narcotics more pronounced in humans than dogs; however, this seems very unlikely in view of present clinical experience. In the animal studies quoted from Murphy and Hug, the same reduction of enflurane MAC was found for comparable levels of fentanyl in the plasma over eight hours.

As Berman and Patel correctly state, it is yet to be determined whether cimetidine increases neonatal pulmonary vascular resistance.

In the final analysis the clinician must, as he so often must, arrive at the best decision with inadequate data. It is my view that the risk of maternal death from aspiration pneumonitis outweighs any hypothetical risk of very short-term cimetidine or ranitidine therapy and that these agents are probably the safest and most efficient means of increasing gastric pH before elective cesarean section.

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Although it may be extremely difficult, similar studies could be carried out in humans to provide useful information on this important question. The application of infusion techniques and predictable plasma levels of short-acting narcotics would provide a useful tool to achieve this end. Until such studies are performed, we must continue to raise the serious question of whether or not more narcotics provide more analgesia.

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