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REFERENCES

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In reply.—As Moir and McMorland state there is usually ample warning of an impending emergency cesarean section so that it is possible to administer epidural anesthesia or one or two doses of cimetidine. At Medical Center Hospital there are 3 or more h warning for 75% of emergeny cesarean sections and a 90-min warning in 81%. The high percentage results from almost all previous cesarean sections being treated by a trial of labor.

However, until we have serum level studies on bupivacaine and lidocaine with and without cimetidine, the administration of cimetidine prior to an epidural is inadvisable, since toxic levels of local anesthetic may result. A clinical trial should be of adequate sample size and should include a large number of underweight parturients, since they frequently need a larger dose of bupivacaine. The epidural doses of bupivacaine and lidocaine for cesarean section are 150–200 mg and 400–500 mg, respectively. These therefore reach the maximum recommended dosages of 200 mg for bupivacaine and 500 mg for lidocaine. Serum levels following epidural anesthesia in the parturient may be increased because of the vascularity of the epidural space and may be close to those following intercostal block in the nonpregnant patient. McGuiness et al. recorded mean blood levels of 720 ng/ml following 160 mg of bupivacaine used for epidural block for cesarean section.

Although ranitidine is an excellent H₂ blocker with a longer duration of action than cimetidine, side effects have been described. There are several reports of reduced hepatic blood flow, evidence that it inhibits cytochrome P 450, and findings that suggest the possibility of interactions with drugs metabolized in the liver, as well as documentation of such interactions in the case of fentanyl, midazolam, and propranolol. In addition to interactions with other drugs, cimetidine also has been associated with cardiac arrest. The few failed epidurals for cesarean section, which may be kept to a minimum by always injecting the local anesthetic through the needle and not the catheter, may be given sodium citrate before operation. This could be combined with an H₂ antagonist given intramuscularly if there is sufficient time.

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REFERENCES
More about the Pharmacokinetics of Vecuronium and Pancuronium

To the Editor:—Cronnelly and his colleagues have reported a comparison of the pharmacokinetics and pharmacodynamics of vecuronium and pancuronium. I believe there are two problems with the articles that commonly are found in many similar articles.

First, they report the results of fitting the plasma concentrations of drug to a three-compartment model. The half-life of the fastest component with both drugs is of the order 2.5 min. However, on examining their sampling schedule they only obtained their first blood samples 10 min after the end of the infusion of the neuromuscular-blocking drugs. By this time, the rapid distribution phase would be about 94% complete. How much better a fit do they get using the three-compartment model rather than a two-compartment one?

Secondly and more importantly, the authors do not give all the parameters of the models they use. I believe that if pharmacokinetic and dynamic analysis is to be of use, then it must not only be descriptive of the results obtained in any one investigation but allow predictions of what may happen when different techniques of using the drugs are employed. With a three-compartment model it becomes necessary to give not only the three half-lives but also the three volumes. Better still would be the publication of all the intercompartmental rate constants.

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In reply: Dr. Norman has raised two questions with respect to our study. First, are the data really better characterized by a three-compartment model rather than a two-compartment model? We used the technique of Boxenbaum, which employs an F test to determine statistical preference for the number of compartments required to best characterize the data. To demonstrate this by visual comparison, the concentrations of pancuronium measured in a patient are displayed in figure 1, along with the fitted functions generated with the two- and three-compartment models. The three-compartment model obviously characterizes the concentration-versus-time data “better” than the two-compartment model.

The second question raised by Dr. Norman involves our ability to characterize the distribution phase using our sampling schedule. Venous blood samples were obtained both during the infusion (at 2, 4, 6, 8 and 10 min) and at 5-min intervals for 20 min following the infusion. Perhaps this was misread by Dr. Norman. The pharmacokinetic model was modified for the drug infusion...