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In Reply:—As noted in our article,[1] we are in complete agreement with Drs. Morishima and Whittington's assertion that there are significant pharmacokinetic differences between humans and sheep with respect to cocaine metabolism. However, the object of our study was to understand the pharmacodynamic impact of chronic cocaine exposure, not the pharmacokinetics of cocaine metabolism, and, despite the pharmacokinetic differences between sheep and humans, the pharmacodynamic effects of cocaine are remarkably similar.

For example, Morishima's laboratory found that sheep demonstrate a gradually diminishing hemodynamic response to repeated short-term cocaine boluses (personal communication). This identical pharmacodynamic phenomenon has been clearly demonstrated in humans and other mammals as well.[2] Similarly, sheep demonstrate sensitization to the locomotor and stereotypic effects of cocaine, just as do animals with more human-like cocaine metabolism.[3] Too, after only 4–6 days of cocaine exposure, sheep clearly demonstrate "drug seeking behavior," as do other species whose pattern of cocaine metabolism more closely resembles humans. Therefore, whereas the ovine model may well be a poor choice to model human cocaine pharmacokinetics, there are ample data to support the use of sheep as a pharmacodynamic model. Consequently, we believe our finding of a reversible increase in isoflurane MAC after chronic cocaine exposure in sheep is qualitatively applicable to humans.

Morishima and Whittington also suggest that we should have "kept plasma cocaine concentrations in the range occurring in human "binge" users." We disagree for two reasons. First, human cocaine use patterns are extremely varied, so it is simply not possible to identify a cocaine plasma concentration that is "representative" of the typical human binge. Second, the purpose of the binge was to study the consequences of repeated short-term cocaine exposure in the absence of a significant plasma concentration of cocaine. Consequently we waited 3 h after the last cocaine bolus to measure MAC. This was done to mimic the increasingly common situation of a patient presenting for surgical repair of a traumatic injury associated with cocaine abuse.[4] By the time many of these patients arrive in the operating room, several hours may have elapsed since their last cocaine dose. Therefore, their plasma cocaine concentrations may be physiologically insignificant at that point, but the physiologic consequences of their preceding binge may not be.

Finally, as Morishima and Whittington point out, the duration of cocaine exposure for any given cocaine dose is shorter in sheep than in humans. If anything, this fact should have biased our study *against* finding a pharmacodynamic effect of chronic cocaine use on MAC. Therefore, that we clearly demonstrated a reversible increase in MAC after chronic cocaine exposure in this model strongly suggests that the same qualitative effect of cocaine can be expected in humans.

Again, we appreciate the valid issues raised by Morishima and Whittington, and we agree that sheep, like all animal models, have shortcomings. However, for the reasons presented earlier, we do not think these shortcomings invalidate the qualitative applicability of our data to humans.

Christopher M. Bernards, M.D.
Associate Professor
Bruce F. Cullen, M.D.
Professor
University of Washington School of Medicine
1959 NE Pacific Street
Box 356540
Seattle, Washington 98195-6540

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Epidural Catheter Insertion and Satisfactory Analgesia —The Mobile *Versus* the Immobile Patient

To the Editor:—The distance a catheter is inserted into the epidural space, whether it be 1 or more cm, does not guarantee satisfactory analgesia. What does result in satisfactory analgesia is whether the catheter remains in the epidural space. If an epidural block immobilizes the patient as for surgery and if the catheter is to be removed immediately after the operation, the distance it is inserted may be 1 cm or more. If the patient is not immobilized, as may occur in obstetrics or when used to relieve postoperative pain, then enough of