TABLE 1. Comparison of Experimental Conditions in Animal Trials in Which Sufentanil Was Administered Intrathecally or Epidurally

Species	Route of Administration	Mean Dose (μg/kg)	Volume (ml)	Frequency	Spinal Cord Pathology	Reference
Sheep	Intrathecal	1.5–7.5	4.2–0.8	4×/day for 3 days	Yes	1
Rat	Intrathecal	0.2–60	0.01	1×	†	2
Cat	Intrathecal	1–100	0.2	1×/day during 5 days	Yes	2
Dog	Epidural	1.5–10	2.0	1×/day for 15 days	Yes	3
Guinea pig	Epidural	2,500	0.25	1×/day for 7, 14, 28 days	Yes	*

† Not investigated.

the observed spinal damage—especially so if a hypotonic highly lipophilic substance (sufentanil) is compared to an isotonic hydrophilic control (saline). Moreover, inflammatory changes at the catheter insertion were observed in the saline-injected sheep.[1]

In addition to these differences in injection techniques, species differences may exist. After an intrathecal injection of local anesthetics, Rosen *et al.*[5] reported neurologic deficits in sheep but not in monkeys. The widespread use of spinally administered local anesthetics in humans is also inconsistent with the reported toxicity in sheep. In conclusion, these data indicate that extrapolations of toxicity data from sheep to humans should be done very cautiously and that clinical and experimental data, in more commonly used laboratory animal species, give no evidence of any drug-related spinal toxicity. Spinal toxicity is even more unlikely to happen with the isotonic solution of sufentanil, which has recently been made available for spinal and intravenous application.

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In Reply:—Van Deun *et al.* suggest that the neurotoxic changes described by us may be due to large volumes of injectate, species differences, and frequency of injections. For evaluation of the neurotoxic potential of a drug, it is important to investigate histologic and functional changes. The absence of histopathologic changes alone is not sufficient to absolve a drug from possible neurotoxic effects. Conversely, it is possible for behavioral effects not to be observed and toxicity still to be present.[1] In our study, there was a general correspondence between the degree of behavior change and the degree of histologic change.

In the study mentioned by Van Deun *et al.*, motor dysfunction and catalepsy were noted in all rats receiving 10 or 30 μg intrathecal sufentanil. In fact, a mortality of 20% was noted in rats receiving 10 μg, and a mortality of 60% was noted in rats receiving 30 μg sufentanil intrathecally.[2] Similarly, in cats receiving 100 μg intrathecal sufentanil, excitation, labored breathing, and hindlimb motor weakness (lasting 2 h) were noted. Intrathecal administration of 300 μg sufentanil resulted in convulsions and death after 7 h.[2]

We agree with Van Deun *et al.* that a large volume of drug can conceivably increase cerebrospinal fluid pressure and cause neurologic deficit. However, we noted a dramatic difference in the behavioral responses between animals receiving large but identical volumes of saline or opioids. When an identical volume of saline was injected intrathecally in animals who had recovered from moderate to severe behavioral effects of sufentanil and butorphanol, no behavioral changes occurred. This suggests that the behavioral and neurologic changes in our study were not due to barotrauma after the administration of large volumes of injectate.

The authors suggest that neurotoxicity may have been related to the frequency of injections. We injected the drugs every 6 h, *i.e.*, four times a day for 4 days, instead of the more usual single daily administration for 1–2 weeks. This was done because of the short duration of action of these drugs and because this closely parallels the use of these opioids in clinical practice. However, this administration schedule was used only in the low-dose sufentanil group. Because of major behavioral changes and prolonged motor weakness of hindlimbs after

every injection of a large dose of sufentanil, it was considered inappropriate to proceed with the large-dose protocol. Therefore, these animals received a total of only two to four injections of intrathecal sufentanil. Thus, neurotoxicity clearly was not related to the frequency of drug administration.

We would like to emphasize that opioid neurotoxicity also may be route-dependent. Our study has shown that drugs that are harmless in the epidural space may be neurotoxic when administered intrathecally by accident or by design. Several case reports of accidental administration of a variety of solutions in the epidural space resulting in only minor or transient symptoms demonstrate the remarkable efficacy of the dura as a barrier to the deleterious effects of drugs.[3,4] Thus, the lack of neurotoxicity in patients receiving very large doses of epidural sufentanil for cancer pain is not strictly relevant.

It should be noted that in one 80-yr-old healthy patient scheduled for cystoscopy, intrathecal sufentanil caused severe respiratory depression and cardiac arrest. No motor weakness was reported in this patient. The patient had accidentally been administered 100 μg sufentanil instead of the intended 10 μg. He was successfully resuscitated; however, he became disorientated and agitated. The disorientation and amnesia lasted several days. The patient was discharged from the hospital without any sequele 6 days after surgery.[5]

We agree with Van Deun *et al.* that species differences may exist and that one must be careful in extrapolating animal data to humans. However, we cannot ignore data that shows that very large doses of intrathecal sufentanil are neurotoxic in rat and cat[2] and in sheep.[6] Our study has shown that a drug that may be safe in the epidural space may not be safe intrathecally. We believe that large doses of intrathecal sufentanil may have a neurotoxic potential in humans. Clearly, further studies are necessary. We have not studied the new isotonic sufentanil solution and therefore have no views on its safety.

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Retrograde Wire-guided Direct Laryngoscopy in a 1-month-old Infant

To the Editor:—Passing a wire retrograde through the cricothyroid membrane and cords and into the pharynx to serve as a guide for an endotracheal tube is an option for airway management in both adults and children in whom tracheal intubation is difficult.[1–5,*] Audenaert *et al.* recently described retrograde-assisted fiberoptic tracheal intubation in children, including several small infants.[3] Since a small-diameter flexible laryngoscope was not available to us, we used a modification of this technique to intubate the trachea of a 1-month-old infant.

A 1-month-old 3.6-kg girl required a gastrostomy tube and Nissen fundoplication because of poor feeding and gastroesophageal reflux. The child was known to have a chromosomal abnormality (2q−). On physical examination, microphthalmia, a recessed chin, anterior larynx, cleft palate, and systolic murmur were noted. The child's surgery was originally scheduled 1 week earlier but had to be cancelled after several attending anesthesiologists were unsuccessful in performing an awake, oral intubation. Most reported that they could not see normal airway structures. On the day of surgery, while the infant was still in the neonatal intensive care unit, awake oral intubation was attempted by an attending neonatologist, who was also unsuccessful. Because of these multiple unsuccessful attempts at awake oral intubation by skilled personnel, we decided to try a retrograde approach.

The child was brought into the operating room, where monitors were placed and intravenous access started. Intravenous glycopyrrolate 0.05 mg was given to dry oral secretions, while intravenous ketamine 5 mg and midazolam 0.1 mg were given for sedation. Spontaneous breathing was maintained throughout the procedure, while oxygen was insufflated over the child's face. A roll was placed under the shoulders to extend the head slightly. The skin over the cricothyroid membrane was cleaned with alcohol; a 1% lidocaine wheal was raised; and an 18-G needle inserted through the membrane with the bevel pointing cephalad. Tracheal placement was confirmed by aspirating air with a 3-ml syringe, after which 0.25 ml 1% lidocaine was injected to anesthetize the vocal cords. The syringe was then removed, and an Arrow

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