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In Reply:—We appreciate the opportunity to reply to the letter of Dr. Agoston. We are pleased that the description of our two cases has generated so much interest. On the other hand, we believe the temptation to overinterpret our two complicated cases should be resisted. Nevertheless, we will respond to the concerns of Dr. Agoston that we did not adequately analyze the various possibilities of the prolonged paralysis we observed.

We agree that a complete differential diagnosis of prolonged weakness in critical care patients is complicated. However, Dr. Agoston offers no substantive new thoughts regarding the cause. As we stated in our response to Dr. Bachenberg,[1] neostigmine transiently reversed the weakness, which lead us to conclude that a neuropathy or a "Guillain-Barre" type of syndrome was not the diagnosis. A neuropathy certainly does occur in critically ill patients[2] and may have been a contributing, but not a primary, factor.

In addition, because we did not find the other classical causes that could have explained the prolonged neuromuscular blockade (pharmacologic potentiation of neuromuscular blockade, residual levels of vecuronium, acidosis, hypokalemia, hypocalcemia, and hypermagnesemia), we measured the plasma concentrations of vecuronium's putative metabolites. We found very high and persistent levels of 3-desacetylvecuronium, which is 50% as potent as vecuronium as a neuromuscular blocking agent in cats. We therefore concluded that accumulation of 3-desacetylvecuronium was the likely cause of the prolonged paralysis.

Dr. Agoston's concern about the validity of our gas chromatography assay findings, given the lack of blank plasma samples, is reasonable. The specificity of the gas chromatography assay for quaternary ammonium compounds arises from the selectivity of the sample processing, the resolving power of capillary column gas chromatography, and the ability of the nitrogen–phosphorous (NP) detector to respond only to components containing nitrogen or phosphorous.[3] In general, we have found that most other nonquaternary ammonium drugs are removed by sample processing during the prewash or do not form extractable ion pairs with iodide ion. In the rare cases in which we have observed recovery of other nonquaternary ammonium drugs after sample processing, their molecular weights or polarities have been sufficiently different from that of vecuronium or its metabolites to allow complete separation by gas chromatography. Among the drugs specifically tested for interference are atracurium, thiopental, fentanyl, midazolam, diazepam, and vancomycin at the 1-μg/ml level. Nonetheless, analysis of samples from critically ill patients provide unusual analytical challenges not only because of the wide variety of drugs given to these patients, but often also because of elevated plasma levels of endogenous components, particularly in patients with liver and kidney failure. To eliminate concerns about the validity of the gas chromatography data from intensive care unit (ICU) patients, we analyzed selected samples from the gas chromatography analysis by selected ion monitoring gas chromatography mass spectrometry at m/z 557, which is the M^+-57 fragment of the tert-butyldimethylsilyl derivative of 3-desacetylvecuronium. In these experiments, the response at m/z 577 was found to be consistent with that found by gas chromatography, and thus the identity of the 3-desacetylvecuronium peak was confirmed.

Dr. Agoston mentions the very interesting problem posed by the study of the pharmacology of 3-desacetylvecuronium in animals, which strongly suggests that 3-desacetylvecuronium is eliminated mainly by the liver.[4] These animal data should not bias his analysis of our first case report. The patient who remained paralyzed 7 days after discontinuation of vecuronium did not have liver impairment. The very slight perturbation of liver function tests observed are common in the ICU setting, and there was no sign of either liver injury (normal to twofold increased levels of transaminases and normal levels of alanine aminotranferase, throughout the period of prolonged paralysis) or of decreased liver synthesis function (normal prothrombin time throughout prolonged paralysis). The direct bilirubin concentration was slightly elevated during the period of prolonged paralysis, but the value observed 24 h before the discontinuation of vecuronium was normal (total bilirubin = 1.2 mg/dl). Because of its very slight elevation and because the alkaline phosphatase plasma concentrations remained normal throughout the period of prolonged paralysis, we consider the slight increase in bilirubin plasma levels not clinically significant. Therefore, we excluded liver impairment as a cause of 3-desacetylvecuronium accumulation (high, stable concentrations of 3-desacetylvecuronium during the last 5 days of prolonged paralysis). On the other hand, we observed a creatinine clearance of 5 ml/min, indicating renal failure. We also observed a very low creatinine clearance (3.6 ml/min) in our second case, a 40-h, prolonged neuromuscular blockade after discontinuation of a 48-h-long administration of vecuronium, in which the patient also had high plasma concentrations of 3-desacetylvecuronium. This suggested that renal failure may be related to 3-desacetylvecuronium accumulation. This apparent contradiction between human observation and animal data cannot be explained until there is an animal model with which to study the effect of long-term administration of vecuronium on its pharmacokinetics.

We feel confident of our conclusion that prolonged neuromuscular blockade can occur after prolonged administration of vecuronium, and that it may be due to the accumulation of the metabolite 3-desacetylvecuronium.

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Complication of Continuous Spinal Microcatheters: Should We Seek Their Removal If Sheared?

To the Editor:—The use of continuous spinal microcatheters is becoming more frequent. Hurley and Lambert[1] described their efforts regarding the use of a 27-G microcatheter. In their report they noted an incidence of 2 of 58 microcatheters breaking. No reports or guidelines exist regarding the management of broken microcatheters or whether they should be regarded as different from epidural catheters. Often quoted is the recommendation by Bromage[2] not to attempt surgical removal of a sheared epidural catheter.

In a recent case at our hospital, a patient received continuous spinal anesthesia for a left inguinal hernia repair. Insertion of the spinal catheter (28-G) through a 22-G spinal needle was accomplished using the CoSPAN Continuous Spinal Tray made by the Kendall Company and with the patient in the left lateral decubitus position. At the completion of the surgical procedure, the patient was fully flexed while sitting during removal of the microcatheter. Resistance was met during removal, and the microcatheter broke at the skin level. A second attempt to remove the catheter using a hemostat failed, with the catheter stretching before retracting below the skin line. Portable x-ray of the area was not helpful in locating the microcatheter. The patient was then placed in the prone position on a Wilson frame to facilitate flexion of the lumbar area. After making a small surgical incision, the catheter segment was easily found at the subcutaneous tissue level and extracted without any noticeable traction on the broken catheter segment. The surgical procedure for removing the microcatheter segment lasted less than 5 min.

Fear of catheter breakage or shearing is a major concern when using the newer microcatheters for continuous spinal anesthesia. Baxter[3] reports the shearing of a microcatheter during an attempt to remove it, leaving a 5–6-cm segment of catheter within the patient. The microcatheter was not visualized radiographically, and therefore it was elected not to attempt to surgically locate and extract it.

We believe that an important distinction should be made between sheared epidural catheter tips (which usually are sheared while attempting to withdraw a catheter through the epidural needle) and broken continuous spinal microcatheter segments (which are sheared while attempting to withdraw the catheter after completion of the surgical procedure). In contrast to epidural catheters, the spinal microcatheter segment may still be located partially within the subarachnoid space. Theoretically, this would provide a conduit for continued leakage of cerebrospinal fluid. We believe that a simple surgical attempt to retrieve the microcatheter segment is not unreasonable. Use of a Wilson frame or similar structure facilitates catheter removal by allowing the lumbar area to be flexed.

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