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In reply:—It was our intention to alert readers that we had developed an assay that could detect sufentanil and its metabolites in the 50–200 picogram range. All our prior studies to detect sufentanil by packed-column gas chromatography had been hampered by poor sensitivity and the appearance of interfering substances in the chromatographic profiles.[1] Thus, we considered this a major, reportable discovery. To our knowledge there is no published technique for ready detection of sufentanil at the levels commonly used for anesthesia.

We stated in the discussion that the use of this assay for pharmacokinetic studies will be difficult because the terminal elimination phase of sufentanil is at or less than the limits of detection. As we suggested,[2] we are currently analyzing larger plasma samples to increase our sensitivity and are not experiencing any problems with interfering substances. It should be noted that we have used this assay for drug abuse and overdose cases as well as patient studies (cardiac and chemotherapeutic) where higher doses of sufentanil are administered. In these analyses, we have found the assay quite adequate in the range of 100–200 picogram sufentanil/ml plasma.

The extraction efficiency and coefficient of variation in the early stages of our assay were not ideal. The extraction efficiency for sufentanil from serum is 77–82%. Extreme care must be taken to minimize evaporation or physical losses during the reconstitution of the extracted sufentanil into microliter volumes of toluene. The coefficient of variation for 5,000, 1,000, 500, 100, 50, and 25 picograms/ml of sufentanil in serum was 13% (3), 7% (6), 15% (8), 21% (6), 35% (7), and 42% (4), respectively, with the N-value indicated in parentheses. We are currently trying to increase our precision and accuracy along with increasing our sensitivity.

We cannot offer a satisfactory explanation for the rapid drop in plasma sufentanil concentrations between 13 and 17 h in the chronic renal failure patient.[2] The complications we reported were not unique to this patient, because a second chronic renal failure patient experienced respiratory depression. However, with this patient, the plasma sufentanil concentrations were within those found for control patients.[2,3] We have since terminated our studies using sufentanil in renal failure patients until a suitable explanation for the complications can be found.

Because there are no published studies concerning the metabolism of sufentanil, primarily due to the previous absence of suitable assays for sufentanil and its metabolites, we felt at liberty to speculate on its metabolism. Because the major metabolic pathways for alfentanil and sufentanil are similar,* it did not seem inappropriate to apply the possibility of polymorphic metabolism.[4]

Our articles and the letter by Avram *et al.* emphasize the need for cautious use of this potent anesthetic. The use of an agent that has one published pharmacokinetic study,[3] one published analytical assay,[2] and no published metabolic studies should be of considerable concern.

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* Meuldermans W, Hurmans R, Hendricks J, Woestenborghs R, Thijssen J, Lenaaerts F, Heykants J: Plasma levels, excretion and metabolism of tritium-labeled sufentanil after intraveneous administration in dogs. Janssen Preclinical Research Report R33, November 1980, pp 800–808.

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Reliability of Sufentanil Plasma Level Assays in Patients

To the Editor:—We would like to comment on the recent articles by Weldon *et al.*[1] and Wiggum *et al.*[2] concerning sufentanil plasma levels in patients. In the first article, the authors describe a capillary gas chromatographic (GC)