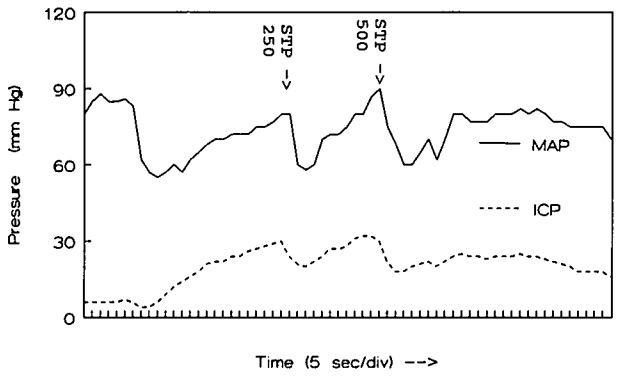

FIG. 1. ICP response to reperfusion and sodium thiopental (STP).

A 22-yr-old man was admitted to our institution in fulminant hepatic failure of unknown etiology. He rapidly developed stage 3–4 hepatic coma, and as ventricular size was small, a modified Richmond subarachnoid bolt was inserted for monitoring of ICP. An initial pressure of 36 mmHg was noted. The following day an orthotopic liver transplant was performed. During the preanhepatic and anhepatic stages of the procedure, the patient's ICP remained below 10 mmHg with only moderate hyperventilation (P_{CO_2} 27). Upon completion of the anastomoses of the graft liver, as the portal vein was unclamped, an immediate decrease in mean arterial pressure (MAP) occurred. As the MAP spontaneously returned to baseline, the patient's ICP began to increase. Manual hyperventilation was instituted with little effect. When the ICP reached 30 mmHg, thiopental was administered intravenously in two bolus doses of 250 mg and 500 mg, respectively (fig. 1). The patient's ICP transiently decreased to 20 mmHg, but rapidly returned to 33 mmHg. Following the second dose of thiopental, the patient's ICP remained below 24 mmHg and continued to slowly decline to 4 mmHg by the end of the procedure. No further treatment of the ICP was instituted other than continued moderate hyperventilation (P_{CO_2} 32 mmHg). No vasopressors were administered during the case. In the ICU the patient's ICP remained 10–13 mmHg and the bolt was removed on the second postoperative day. The trachea was extubated on that same day. No neurologic sequelae were present 1 week postoperatively.

The incidence of cerebral edema in patients with fulminant hepatic failure has been reported to be over 50% with evidence of herniation at the time of death in 12%.[2] Cerebral edema has been considered the most common immediate cause of death in fulminant hepatic failure.[3] Thus, treatment of cerebral edema and its resultant increased intracranial pressure is a critical element in managing cases of hepatic failure. Brajtbord *et al.* have reported a case of elevated intracranial pressure during OLT that was treated by incremental removal of CSF *via* a ventriculostomy.[4] The etiology of this increase was unclear, however, because vasopressors had been given to treat hypotension at the time of the increase in ICP. As our patient did not receive any form of vasopressors, the acute increase in ICP seemed to be the direct result of reperfusion of the graft liver and/or ischemic mesentery and lower extremity tissues. Data concerning a "safe" upper limit for ICP are sparse, but is has been suggested that a persistent level over 30 mmHg should be treated to reduce the risk of herniation.[5]

We have observed this same phenomenon in several, but not all, patients in fulminant hepatic failure undergoing hepatic transplantation. Our experience, along with the other reports cited, suggests that reperfusion of ischemic tissues may have an adverse effect on the intracranial pressure of a patient with reduced intracranial compliance. Early diagnosis and treatment of such may avoid a potentially devastating outcome.

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Pre-Eclamptic and Healthy Term Pregnant Patients Have Different Chronotropic Responses to Isoproterenol

To the Editor:—We have previously demonstrated that healthy term pregnant women have a blunted chronotropic response to isoproterenol compared to nonpregnant women.[1] If pre-eclamptic and healthy term pregnant patients differ in chronotropic responsiveness to isoproterenol, an isoproterenol epidural anesthesia test dose designed for healthy parturients might be unsafe or not efficacious in pre-eclamptic patients. We therefore determined the chronotropic responsiveness of pre-eclamptic patients to isoproterenol and compared these data with those previously obtained from healthy term pregnant and nonpregnant women.[1,2]

With IRB approval, we obtained written informed consent from five nonlaboring, nulliparous, term pregnant patients with mild pre-eclampsia. All patients had new onset proteinuria (≥ 2+ by urine dipstick on two occasions) and a recent (<2 week) diastolic blood pressure (BP) increase of ≥ 15 mmHg and/or systolic BP increase of ≥ 30 mmHg on two occasions at bed rest 6 h apart. Preinjection external

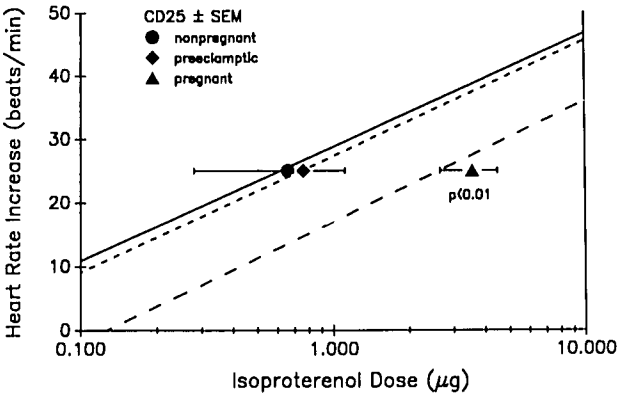

FIG. 1. The chronotropic response to isoproterenol in pre-eclamptic pregnant, healthy pregnant, and nonpregnant women. Mean regression lines were interpolated from individual dose-response curves. Data for healthy pregnant and nonpregnant women were obtained previously. The CD25 in pre-eclamptic patients (0.8 μg) was significantly less than the CD25 in healthy pregnant patients (2.6 μg) but did not differ from the CD25 in healthy nonpregnant patients (0.7 μg). The slopes of the mean regression lines did not differ significantly.

fetal heart rate (FHR) tracings were normal (FHR >120 and <160 beats per min with normal long-term variability, 5–10 beats per min short-term variability, and no decelerations). While participants rested quietly in a supine position with left uterine displacement, we continuously infused 0.9% saline. We recorded BP every minute and continuously recorded maternal heart rate (MHR), FHR, and uterine contractions.

After recording baseline measurements, we administered incremental bolus iv injections of isoproterenol (0, 0.1, 0.25, 0.5, 1, and 2 μg) until the MHR increased 25 beats per min above baseline (CD25) for ≥ 15 s. We waited until 5 min after the MHR had returned to baseline before injecting the next dose. As in our previous study, all drugs were prepared and administered by the same two authors (BLL and CAD). An obstetrician (MJD) analyzed the FHR tracings for signs of fetal distress (short-term FHR variability ≤ 5 beats per min, > 1 late deceleration, or a change in baseline FHR to ≤ 120 or ≥ 160 beats/min).

We estimated each patient's CD25 by log interpolating between the neighboring isoproterenol doses. We compared the group geometric mean CD25 with CD25 values previously obtained for healthy term pregnant and nonpregnant women using Student's *t* test with Bonferroni correction.[1] One-way ANOVA for repeated measures and Dunnett's test determined the significance of BP changes following the isoproterenol doses that surrounded the CD25. $P < 0.05$ indicated significance.

The mean CD25 in preeclamptic patients (0.8 μg with a coefficient of variation of 102%) differed significantly from the CD25 previously determined for healthy term pregnant patients (3.6 μg with a coefficient of variation of 51%) ($P < 0.01$) but did not differ from the CD25 previously determined for healthy nonpregnant women (0.7 μg with a coefficient of variation of 130%) (fig. 1). Systolic and diastolic BP and FHR patterns did not change.

The fivefold difference in the chronotropic responsiveness of pre-eclamptic and healthy pregnant women may complicate efforts to design a chronotropic epidural anesthesia test dose that is both safe and effective in all parturients. Isoproterenol 5 μg safely and effectively indicates iv injection in healthy pregnant women.[3] However, isoproterenol 5 μg, which is 1.4 times the CD25 for healthy term pregnant women, is 6.25 times the CD25 for pre-eclamptic term pregnant women. Isoproterenol 5 μg is more likely to cause hypotension or exaggerated tachycardia in a pre-eclamptic woman than in a healthy pregnant woman.

Of course, isoproterenol cannot yet be used in an epidural anesthesia test dose even in healthy term pregnant women, for insufficient animal neurotoxicology data exist.

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Propofol Causes Cardiovascular Depression. I.

To the Editor:—In the otherwise exhaustive and excellent review of the new iv anesthetic propofol, Sebel and Lowdon[1] confused at least this reader about the cardiovascular effects of the drug. As one of the FDAs consultants, particularly on the cardiovascular effects of propofol, I have had the opportunity to review both the company's studies and the published literature in some detail. In my opinion, all of the studies that have looked at the effect of propofol on cardiovascular dynamics in a variety of populations have demonstrated that propofol produces cardiovascular depression that is very similar to that of the iv barbiturates (thiopental and methohexital). When differences have been demonstrated, propofol has almost universally been more depressant to the cardiovascular system than are the iv barbiturate-induction agents. Although Sebel and Lowdon note that cardiac output and arterial pressure were significantly and markedly decreased in a number of studies, several of their statements, I believe, may be misleading.

For instance, the statement that, "The cardiovascular effects of pro-