

findings suggest that diazepam and droperidol may be better supplements than nitrous oxide during morphine anesthesia. Whether diazepam or droperidol produces as much amnesia as nitrous oxide after 2 mg/kg morphine must still be determined. However, the low incidence of intraoperative awareness (1 in 29) in this study is encouraging preliminary evidence that small amounts of either drug may be effective as an amnesic supplement during morphine anesthesia.

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## Prolonged Response to Succinylcholine Following Pancuronium Reversal with Pyridostigmine

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We recently had a case in which recovery from succinylcholine-induced paralysis was delayed after administration of pyridostigmine to reverse the action of pancuronium.

## REPORT OF A CASE

An 82-year-old, 55-kg man who had a six-month history of weight loss (18 kg) was scheduled for an elective exploratory laparotomy. Preoperative laboratory data included hemoglobin 12.5 g/100 ml, total protein 5.9 g/100 ml, albumin 2.0 g/100 ml, creatinine 0.9 mg/100 ml, total bilirubin 21.4 mg/100 ml, direct bilirubin 15.6 mg/100 ml, SGOT 209 units, and alkaline phosphatase 305 units. Serum electrolytes were normal and prothrombin time was 70 per cent. The patient was not taking medications regularly, but received vitamin K preoperatively.

In the operating room, self-adhesive conductive pads were placed over the ulnar nerve at the wrist and elbow and attached to a peripheral nerve stimulator (Block-Aid Monitor, 50 Hz), an electrocardiogram was attached, and a radial-artery catheter was placed using local anesthesia. Anesthetic induction was started at 7:45 A.M. with gallamine, 20 mg, iv, followed 3 minutes later by thiopental, 150 mg, and succinylcholine (SCh), 120 mg, iv. An 8-mm orotracheal tube was placed but an unsatisfactory tracheal seal led to the decision to replace the tube. Two additional 60-mg doses of SCh were administered for reintubation with a 9.0-mm orotracheal tube. Anesthetic maintenance was with nitrous oxide-oxygen (4:2) plus incremental doses of fentanyl. At 8:15 a sustained response to tetanus was present. Pancuronium, 3 mg, at this time abolished visible twitch response, but by 9:30 the response was judged sufficient to justify an additional dose of pancuronium. In anticipation of a prolonged operation an additional 2 mg was given. However, following discovery of a large hepatic duct tumor, the surgeons merely placed a T-tube and began abdominal closure. Pyridostigmine, in divided doses of 15, 5, and 10 mg, was administered with atropine between 9:55 and 10:10. Sustained tetanus and spontaneous ventilation were

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present at 10:15, and the tracheal tube was removed. The total dose of fentanyl was 400  $\mu$ g, administered between 7:55 and 9:30. The patient was awake and ventilation was adequate, so no narcotic reversal was administered.

Before transferring the patient to the postanesthesia recovery room, the surgeons elected to place a catheter in the bladder—preoperative attempts had been unsuccessful. Placement was not successful and it was decided to perform a suprapubic cystostomy. Therefore, at 11:15 the patient received gallamine, 20 mg, followed 3 minutes later by thiamylal, 125 mg, and SCh 60, mg all iv. A minute later muscle relaxation was inadequate for tracheal intubation, so an additional 30-mg dose of SCh was administered. An orotracheal tube was placed and anesthesia maintained with nitrous oxide and fentanyl (total dose 100  $\mu$ g).

The operation ended at 12:30 and the patient still had no twitch response. He was taken to the postanesthesia recovery room and mechanically ventilated with 40 per cent oxygen. A twitch response was visible by 1:00 P.M. At 2:25 (190 minutes since the last dose of SCh) a weak response to tetanus was followed by fade. At this time, edrophonium, 5 mg, plus atropine, 0.5 mg, was administered iv. Within 2 to 3 minutes the patient's grip strength was greatly increased, minute ventilation was 7 l/min, he withdrew his arm when the peripheral nerve stimulator was activated, and he nodded affirmatively when asked whether he was stronger. Neostigmine, 0.5 mg, plus atropine was administered at 2:30, followed by removal of the tracheal tube at 2:35. Blood gases after 15 minutes of spontaneous ventilation breathing 40 per cent oxygen were adequate. An additional "prophylactic dose" of neostigmine, 0.5 mg, plus atropine was given at 2:50. Muscle weakness did not recur.

A blood sample drawn on the third postoperative day revealed a cholinesterase activity of 0.6 units (normal 3–8) and a dibucaine number of 66 (normal 77–83).

## DISCUSSION

Prolonged SCh-induced paralysis may result from drug- or disease-produced reductions in pseudocholinesterase (serum cholinesterase) activity or the presence of an atypical pseudocholinesterase that does not hydrolyze ester linkages. Pseudocholinesterase activity (three days postoperatively) was greatly decreased in our patient, probably reflecting underlying hepatic disease and biliary obstruction. This reduced pseudocholinesterase activity may have contributed to a longer duration of the SCh effect, but prolonged paralysis (more than an hour) is unlikely to result from hepatic disease alone.<sup>1-3</sup> For example, Foldes *et al.*<sup>2</sup> reported the duration of SCh-induced

apnea was increased only two- to threefold in the presence of severe hepatic disease with reduced pseudocholinesterase activity. The dibucaine number of 66 suggested a heterozygotic phenotype with mixtures of both normal and atypical esterases. Heterozygotes destroy SCh less efficiently, but the duration of action of SCh is prolonged only 5 to 10 minutes.<sup>4</sup> Pancuronium has been shown to reduce pseudocholinesterase activity, but this inhibition is probably transient.<sup>5</sup> Thus, a disease- or pancuronium-produced reduction in pseudocholinesterase activity or the presence of a heterozygous phenotype was unlikely to be the only explanation possible for the prolonged SCh-induced paralysis in our patient.

Another possible explanation for the prolonged response to SCh involves the prior administration of pyridostigmine. Cholinesterase inhibitors, including pyridostigmine, have been demonstrated to extend the duration of action of SCh,<sup>6,7</sup> but the mechanism for this response has not been established. For example, the influence of pyridostigmine, if any, on pseudocholinesterase activity has not been reported. However, if the ability of anticholinesterase drugs to prolong SCh action correlates with the duration of their anticholinesterase action, we might anticipate a prolonged response whenever SCh is administered in the presence of background anticholinesterase activity. Miller *et al.*<sup>8</sup> reported that the duration of action of pyridostigmine (9 mg/m<sup>2</sup>) was longer than 80 minutes. Our patient received 30 mg pyridostigmine (about 20 mg/m<sup>2</sup>), and thus a significant anticholinesterase effect was probably still present 65 minutes later when SCh was again injected. Indeed, the absence of prolonged paralysis after the initial injection of SCh suggested that a residual pyridostigmine effect was a possible cause of the subsequent abnormal response to SCh.

Three hours after the last dose of SCh, the picture was that of a desensitization blockade (poorly sustained tetanus). Edrophonium followed by neostigmine produced a persistent reversal of muscle weakness. If the persistent SCh paralysis at this time had still been due to residual anticholinesterase activity the administration of edrophonium should have had no effect or increased muscle weakness. Thus,

the mechanism that may have originally contributed to the prolongation of SCh-induced paralysis (*i.e.*, anticholinesterase activity) was later employed as a successful treatment.

In summary, prolonged paralysis from SCh occurred following pyridostigmine reversal of pancuronium-induced neuromuscular blockade. Because of an initial normal response to SCh, the subsequent prolonged paralysis was attributed to residual anticholinesterase effects of the pyridostigmine.

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## Safety of Brachial Arterial Catheters as Monitors in the Intensive Care Unit—Prospective Evaluation with the Doppler Ultrasonic Velocity Detector

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At the University of Iowa, all patients undergoing open-heart surgery are monitored during and after operation with brachial arterial percutaneous cannulas inserted prior to induction of anesthesia. Clinically there has been no significant complication as a result

of such cannulations. The purpose of this study was to assess the arterial circulation of the upper extremity prospectively with the aid of the Doppler ultrasonic velocity detector to determine the incidences of subclinical and clinical thromboembolic sequelae of this procedure. We have found Doppler ultrasound to be a sensitive index of asymptomatic arterial obstructive complications following cardiac catheterization via both the femoral<sup>1,2</sup> and brachial<sup>3</sup> arterial routes.

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## METHODS AND MATERIALS

From November 1973 to May 1974, 54 patients undergoing open-heart surgery at the University of Iowa Hospitals were studied. There were 36 male and 18 female patients, ranging in age from 6 to 73 years, with a mean of 47 years. Twenty-six patients underwent coronary-artery bypass for ischemic heart disease, 19 patients had correction of acquired