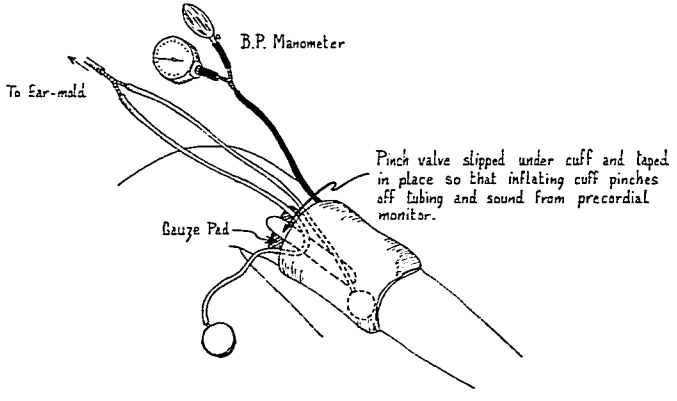

FIG. 2. Valve in place.

The tongue blades are taped together at one end. The applicator stick is taped longitudinally in the center of one of the tongue blades to provide a more discrete compression surface against the rubber tubing. With the tubing placed between the two tongue blades, they are inserted under the blood pressure cuff. The rubber tubing is then connected as shown in figure 2. When the blood pressure cuff is inflated, compressing the tongue blades, the rubber tubing is "pinched off" so that precordial sounds are no longer heard and Karotkoff sounds from the blood-pressure acoustical pickup are clearly audible. With a few adjustments in relative positions of the tongue blades and tubing, it is possible to "pinch off" the sound from the precordial monitor at a pressure of only 20–30 mm/Hg, thus avoiding any overlap in sounds from the precordial monitor and blood-pressure acoustical pickup.

Seizures Induced by Pentazocine

STEPHEN H. JACKSON, M.D.,* CHRISTOPHER DUEKER, M.D.,† LAWRENCE GRACE, M.D.‡

Large doses of morphine (1–3 mg/kg body weight) and other narcotic drugs are being used with increasing frequency for the anesthetic management of patients with severe cardiopulmonary disease. The advantages attributed to this use of narcotic-predominated anesthetic regimens include: 1) minimal myocardial depression [1–4]; 2) reduction or elimination of the requirements for nitrous oxide or other more potent anesthetic drugs; 3) facilitation of early postoperative respiratory care.

Pentazocine (Talwin, Winthrop) is a potent analgesic that also possesses sedative properties and is not subject to narcotic controls. Twenty to forty mg of pentazocine are

* Assistant Professor of Anesthesia.
† Resident, Department of Anesthesia.
‡ Resident, Department of Neurology.
Received from the Departments of Anesthesia and Neurology, Stanford Medical School, Stanford, California.

usually as effective in providing analgesia as 10 mg of morphine, and the duration of action is similar.[5] Pentazocine is a safe preanesthetic medication, supplement to surgical anesthesia, and postanesthetic analgesic.[6] Clinical studies of the cardiovascular and pulmonary effects of usual doses (30–60 mg) of pentazocine indicate that it is a safe substitute for morphine in the therapy of acute myocardial infarction in man.[7, 8]

In view of the favorable information regarding pentazocine and the very favorable experience that we[9] and other anesthetists[1] have had with narcotic-predominated anesthetic regimens, we evaluated pentazocine as a substitute for the more conventional narcotics. In a morphine-predominated anesthetic regimen we routinely administer morphine in a total dose of 1 mg/kg body weight. Because morphine is approximately three times more potent than pentazocine in providing analgesia,[5] we arbitrarily decided to administer pentazocine in a total dose of 3 mg/kg body weight. This dose was injected intravenously at a rate of 10 mg/30–60 seconds, during which time oxygen was administered by mask. A small amount of a potent inhalational anesthetic, (*e.g.*, 1.5 per cent inspired halothane) was then added, as tolerated by the cardiovascular system, until anesthesia was attained. Ventilation was assisted or controlled so as to maintain normocarbia (Pa_{CO_2} 36–44 torr).

Twenty-one patients received this pentazocine regimen, and 19 were anesthetized without complication. However, two patients (numbers 8 and 21 in the series) without known histories of epilepsy developed grand mal seizures during the administration of pentazocine. These two cases are reported and followed by a discussion of the well-established, but rarely encountered, epileptogenic properties of pentazocine.

Report of Two Cases

Patient 1. A 37-year-old woman with acquired mitral valvular disease was admitted to the hospital for a valve replacement. She weighed 52 kg. Her known medical history included mild rheumatoid arthritis, chronic anxiety, and "allergies" to chloramphenicol, streptomycin, and codeine. She was receiving digoxin, chlorothiazide, potassium, and occasional doses of diazepam. On physical examination she was apprehensive, with signs of her cardiac disease, but otherwise normal. Routine laboratory studies disclosed no abnormalities. Preanesthetic medication consisted of 10 mg morphine and 0.5 mg scopolamine given intramuscularly with a prophylactic antibiotic (cephalothin) 75 minutes prior to induction of anesthesia. The patient had received 5 mg diazepam for apprehension five hours earlier in the morning. After preoxygenation and while breathing 100 per cent oxygen, she received 120 mg pentazocine intravenously over eight minutes. Blood pressure was unchanged, pulse had risen from 84 to 100, and respiration was assisted and judged adequate. At this point a generalized tonic–clonic seizure occurred, with convulsive activity lasting approximately 60 seconds. Decamethonium, 5 mg, was administered intravenously and respiration was controlled with 100 per cent oxygen. Two minutes later seizure activity recurred for 30 seconds but was modified by the relaxant. Diazepam, 2.5 mg, was given intravenously. Rectal temperature was 36.8 C. Ventilatory support was continued for an hour, after which the patient was drowsy and confused but ventilating adequately. There were no further convulsive phenomena. Eight hours later her mental status and neurologic examinations were normal. Subsequent questioning of the patient and her family revealed that an unusual syncopal episode with clonic "jerking" (probable seizure) had occurred four months previously, but medical attention had not been sought. In addition, the patient described a lifelong sensitivity to flickering light, manifested by dizziness and a feeling of impending syncope, which could always be aborted by avoiding the stimulus. The patient's mother admitted to a similar photosensitivity, but neither she nor any other known family member had ever convulsed. Roentgenograms of the skull and lumbar puncture disclosed no abnormalities. The electroencephalogram showed a photoconvulsive response to flickering light over a wide range of frequencies. Anticonvulsants were begun and a week later the patient was anesthetized without incident, using a morphine-predominant technique and precautions to avoid exposing her to flickering light in the operating room.

Patient 2. A 46-year-old man with coronary arterial disease and a severe, incapaciting anginal syndrome was scheduled for a double aorto-coronary saphenous-vein bypass procedure. He weighed 84 kg. Five months before he had experienced abrupt left hemiparesis and left homonymous hemianopia during coronoray angiography, which subsequently cleared quickly and nearly completely except for a mild cortical sensory deficit in the left upper limb. EEG then showed mild right hemispheric slowing without paroxysmal features, and carotid angiography was normal. No seizures had occurred since the episode nor was there any previous or family history of epilepsy. Recent medication consisted of nitrites,

bendroflumethiazide, and clofibrate. Physical and neurologic examinations on this admission were unremarkable except for the discovery of extinction of simultaneous stimuli in the left hand. Results of laboratory studies were normal. Preanesthetic medication of 45 mg pentazocine and 0.5 mg scopolamine was given intramuscularly with a prophylactic antibiotic (cephloridine) 75 minutes prior to induction of anesthesia. After preoxygenation and while breathing 100 per cent oxygen, the patient received a total dose of 240 mg of pentazocine intravenously over 12 minutes. The intravenous solution also contained cephalothin. Blood pressure was unchanged, pulse increased from 90 to 130, and respiration was assisted and deemed adequate. After receiving half the total dose of pentazocine, the patient complained of a "warm feeling." After he had received the full 240 mg, a 60-second tonic–clonic seizure without focal features occurred. Decamethonium, 3 mg, was administered intravenously and respiration controlled with 100 per cent oxygen. Rectal temperature was 37 C. Ventilation with oxygen was continued for 45 minutes, after which the patient was able to maintain adequate ventilation and respond to loud verbal stimuli. Seventy-five minutes later he was confused and somnolent, but his neurologic status was as before. An EEG the following day again showed mild right hemispheric slowing without paroxysmal activity. The patient was placed on diphenylhydantoin and phenobarbital and a week later was anesthetized without incident using a morphine-predominant anesthetic technique.

Discussion

Two of 21 patients receiving relatively large doses (3 mg/kg body weight) of intravenous pentazocine developed grand mal seizures. In 1964, paroxysmal electrical activity was recorded by Telford *et al.* in one of three healthy volunteers without histories of epilepsy who received a mean dose of 123 mg of pentazocine intravenously in five to seven divided doses.[10] The single volunteer who developed the paroxysmal activity had received a total dose of 120 mg in 78 minutes, but he did not convulse.[11] Pentazocine's epileptogenic potency was demonstrated when epileptiform EEG activity followed by convulsions was produced in anesthetized humans (nitrous oxide–oxygen–thiopental) upon intravenous administration of 9.2 mg/kg of pentazocine in divided doses (1 mg/kg each dose).[12] We have shown here that large (3 mg/kg) doses of pentazocine may be administered to patients without convulsive sequelae, although we did not monitor electroencephalographic activity. Even more massive doses of pentazocine have been administered without inducing seizures.[13]

In the FDA-approved drug information for pentazocine, under "Precautions," the physician is advised to use "caution" when administering pentazocine to epileptic patients "although no cause and effect relationship has been established."[14] This would indicate that *routine* (recommended) doses of pentazocine may be administered: 1) to normal people without concern for inducing seizures; and 2) to epileptic people with caution. Neither of these conclusions may be applicable for *larger* doses of pentazocine.

Our first patient who convulsed was, in fact, an epileptic, although this was unknown to her physicians. The second patient, though not epileptic, did have an underlying cerebral abnormality, and possibly a lowered convulsive threshold because of it. In addition, both patients had received other drugs (scopolamine and cephloridine), and the possible effects of multiple drug interactions on their development of seizures should be considered. Both patients later received morphine-predominant anesthetics uneventfully, but only after they had been placed on anticonvulsant therapy. The available evidence indicates that morphine, even in large doses, does not possess epileptogenic properties,[10, 15] and, indeed, we have failed to evoke seizures in more than 600 patients receiving morphine in doses ranging from 1 to 6 mg/kg.[9]

We have reported the occurrence of convulsive episodes in two of 21 patients who received large doses of pentazocine. Because of the apparent dose-dependent epileptogenic properties of pentazocine, we believe that it should not be administered in doses larger than those recommended for routine analgesia.

References

1. Lowenstein E, Hallowell P, Levine E, *et al.*: Cardiovascular response to large doses of intravenous morphine in man. New Eng J Med 281:1389–1393, 1969
2. Vasko J, Henney R, Oldham H, *et al.*: Mechanisms of action of morphine in the treatment of experimental pulmonary edema. Amer J Cardiol 18:876–883, 1966
3. Pur-Shadriari A, Mills R, Hoppen F, *et al.*: Comparison of chronic and acute effects of

morphine sulfate on cardiovascular function. Amer J Cardiol 20:654–659, 1967
4. Vasko J, Henney R, Brawley R, *et al.*: Effects of morphine on ventricular function and myocardial contractile force. Amer J Physiol 210:329–334, 1966
5. Paddock R, Beer G, Bellville J, *et al.*: Analgesic and side effects of pentazocine and morphine in a large population of postoperative patients. Clin Pharmacol Ther 10: 355–365, 1969
6. Gerula G, Keeri-Szanto M: Anaesthetic time/dose curves. VII. Experience with pentazocine. Canad Anaesth Soc J 18:84–91, 1971
7. Scott M, Orr R: Effects of diamorphine, methadone, morphine, and pentazocine in patients with suspected acute myocardial infarction. Lancet 1:1065–1067, 1969
8. Lal S, Savidge R, Chhabra G: Cardiovascular and respiratory effects of morphine and pentazocine in patients with myocardial infarction. Lancet 1:379–381, 1969
9. Jackson S: Unpublished data
10. Telford J, Keats A, Crawley J: EEG alterations by analgesics in man. Fed Proc (abstracts) 23:176, 1964
11. Telford J, Keats A, Crawley J: Unpublished data
12. Bauer R, Pretsky I, Walter R: Hallucinations and EEG changes produced by ethoheptazine, propoxyphene, and pentazocine in man. Pharmacologist 7:163, 1965
13. Neuschatz J: Pentazocine: Massive dosage without side effects. JAMA 209:112–113, 1969
14. Winthrop Laboratories: Talwin®, Physicians' Desk Reference to Pharmaceutical Specialties and Biologicals. Twenty-fifth edition. Oradell, New Jersey, Medical Economics, 1970, pp 1507–1508
15. Jaffe J: Narcotic analgesics, The Pharmacological Basis of Therapeutics. Third edition. Edited by LS Goodman and A Gilman. New York, Macmillan, 1965, pp 247–284

CASE REPORT

Anesthetic Management of a Patient with the Shy-Drager Syndrome

CHARLES A. COHEN, M.D.*

In 1960 Shy and Drager[1] described two patients with orthostatic hypotension and primary degenerative disease of the nervous system. The major clinical manifestations of this entity, now known as the Shy-Drager syndrome, are: 1) orthostatic hypotension; 2) parkinsonism; 3) urinary and bowel dysfunction; 4) impaired potency and libido; 5) decreased sweating. About 100 cases have been reported since 1960.[2, 3] A review of these reveals that at least eight patients have undergone surgical operations. Since no analysis of the course of such individuals during anesthesia has been made so far as can be determined, the following case history is presented.

* Resident in Anesthesia, Department of Anesthesia, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104.

Supported (in part) by USPHS Grant 5-P01-GM-15430-04 and by USPHS Research Training Grant 5-T01-CM-00215-13, from the National Institutes of General Medical Sciences, National Institutes of Health.

REPORT OF A CASE

The patient, a 50-year-old man, had first experienced dizziness and loss of consciousness following prolonged standing in 1964. By 1967 he had noted slowed speech, occasional urinary incontinence, and impotence. In July 1969, because of increasing syncopal episodes, he had to stop working. A diagnosis of multiple sclerosis and diabetes mellitus was tentatively made because of an elevated CSF protein and an abnormal glucose tolerance test.

In early 1970 the patient was admitted to the Hospital of the University of Pennsylvania (HUP). At this time he had severe orthostatic hypotension, parkinsonism, urinary incontinence, an elevated CSF protein with normal sugar and no cells, an abnormal glucose tolerance test, and Battey bacilli (Type III) on sputum culture. He was treated with fludrocortisone (Florinef), hydroxyamphetamine (Paredrine), NaCl, isoniazid, and tolbutamide (Orinase). The following values were normal: PBI, serum electrolytes, Ca, P, liver function tests, 24-hour urine collections for VMA and catecholamines, plasma cortisol, nerve conduction time, EEG, EMG, EKG, brain scan, and diffusing capacity of the lung. Vital ca-