this dose given two times approximately 30 minutes apart resulted in neuromuscular blocks with similar durations and recovery times, indicated that this procedure could be used to assess the effects of d-tubocurarine we were measuring, for each patient acted as his own control. Tachyphylaxis such as that found with decamethonium and succinylcholine infusion was not seen. We attribute the absence of tachyphylaxis to the long interval between doses of succinylcholine, which allowed full recovery of neuromuscular transmission.

Our results indicate that although 3 mg d-tubocurarine prevents succinylcholine-induced fasciculations, it decreases the blocking action of succinylcholine considerably. This could have serious consequences when rapid induction techniques are used for patients with full stomachs, when the safety of the method depends on smooth induction and rapid intubation of the trachea.

We assessed neuromuscular block by the magnitude of twitch responses. However, in most subjects spontaneous respiration returned before twitch reappeared, indicating that even before a measurable response can be elicited from the hand muscles certain muscles of respiration are contracting; thus, intubation might be rendered difficult. If it is considered desirable to prevent the fasciculations, increased intragastric pressure, and other possible side-effects of succinylcholine by the use of 3 mg d-tubocurarine, then at least 70 per cent more succinylcholine must be given to ensure consistently adequate relaxation for intubation.

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Hypertension Following 10 Per Cent Phenylephrine Ophthalmic

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Ten per cent phenylephrine (Neo-Synephrine) ophthalmic is widely used in ophthalmologic surgery, both for capillary decongestion

and for pupillary dilatation. Although the cardiovascular effects of parenteral phenylephrine are well-recognized, the systemic effects of the drug when applied topically have received little documentation. Because the drug is often used preoperatively and at the conclusion of ophthalmologic procedures, anesthesiologists may be confronted with these systemic effects. Three cases of severe hyper-

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tension following the use of 10 per cent phenylephrine ophthalmic are reported.

REPORT OF THREE CASES

Patient 1. A 69-year-old woman entered the hospital with a retinal detachment of the right eye. Past history and review of systems were non-contributory. On admission blood pressure was 108/76 torr and the heart rate 88/min. Starting an hour before operation, the patient received one drop each of 10 per cent phenylephrine (3.3 mg) and 2 per cent cyclopentolate (Cyclodol) in the right eye every five minutes for a total of four doses. Cyclopentolate is a synthetic antimuscarinic compound used as a mydriatic and cycloplegic. The patient was premedicated with pentobarbital, 100 mg, hydroxyzine, 50 mg, and atropine, 0.6 mg, im, half an hour before induction of anesthesia. On her arrival in the operating room, the blood pressure was 169/90 torr. Anesthesia was induced with thiopental, 200 mg, and maintained with nitrous oxide, oxygen, and halothane 0.5-1.0 per cent. The blood pressure dropped to 130/90 torr immediately after induction and then returned to 160/90 torr in the next half hour. At the conclusion of the operation, two drops of 10 per cent phenylephrine were instilled in the right eye. On the patient's arrival in the recovery room, the blood pressure was 204/110 torr, pulse rate 100/min. The blood pressure rose in the next 15 minutes to 210/110 torr, then gradually decreased over the next hour and a half to preoperative levels. The morning after operation the blood pressure was 110/70 torr, and the remainder of the postoperative course was uneventful.

Patient 2. A 3-month-old girl weighing 12 pounds entered the hospital for removal of a congenital cataract of the right eye. Abnormal physical findings were limited to the right eye. Starting an hour and a half before operation the patient received one drop each of 10 per cent phenylephrine and 2 per cent cyclopentolate in the right eye every 10 minutes for a total of three doses. Two hours prior to operation, she received one drop of 1 per cent atropine in the right eye, and 45 minutes before induction of anesthesia, 0.2 mg atropine im. Systolic blood pressure was 130 torr on the patient's arrival in the operating room, and anesthesia was induced and maintained with nitrous oxide, oxygen, and halothane. At the conclusion of the operation, three drops of 10 per cent phenylephrine were instilled in the right eye, and within two minutes systemic blood pressure had risen to 230 torr. The patient was transferred to the recovery room, where the systolic pressure was 200 torr after 10 minutes. It then dropped to 140 torr in the next two hours. The evening after the operation systolic pressure was 130 torr. The remainder of the postoperative course was uneventful.

Patient 3. A 62-year-old man entered the hospital for removal of a cataract of the left eye. He denied any previous serious illness, and the review of systems was unremarkable. On admission, blood pressure was 170/110 torr and heart rate 95/min. One and a half hours before operation, the patient received one drop each of 10 per cent phenylephrine and 1 per cent cyclopentolate. Forty-five minutes prior to induction of anesthesia, he received pentobarbital, 75 mg, and hydroxyzine, 50 mg, im. On his arrival in the operating room, blood pressure was 205/105 torr and heart rate 75/min. A retrobulbar block with mepivacaine, 200 mg, was done. However, before the operation could begin, it was noted that the blood pressure had risen to 240/110 torr. The operation was cancelled and the patient transferred to the recovery room, where the blood pressure was 220/110 torr. There was no decrease in the next five minutes, and the patient was given chlorpromazine, 7.5 mg, iv, in three equally divided doses over a 10-minute period. The blood pressure decreased to 170/90 torr during this time, then to 140/90 torr during the next hour. The following morning the patient was premedicated in an identical manner, but the phenylephrine drops were omitted. Blood pressure on admission to the operating room was 160/80 torr. After the retrobulbar block, blood pressure dropped to 140/80 torr and remained at that level throughout the operation.

DISCUSSION

Reports describing adverse systemic reactions to topical application of phenylephrine ophthalmic solutions are rare. Lansche reported a patient who developed severe hypertension and occipital headache after instillation of one drop of 10 per cent phenylephrine. This patient had previously manifested a similar reaction to ophthalmic epinephrine. Reynolds et al. reported a case of extreme hypertension and occipital headache which progressed to subarachnoid hemorrhage following application of a cotton wick soaked in 10 per cent phenylephrine to the lower conjunctival cul-de-sac. Both of these patients recovered without sequelae.

The ophthalmologic use of phenylephrine was first described by Heath. He applied the drug in powder form to the dog cornea and found a sudden and marked increase in systemic blood pressure. However, Heath and Geiter later measured blood pressures in 120 patients before and after the use of phenylephrine eye drops and found only slight in-
creases in blood pressure in 2 per cent of the patients. When McReynolds et al. instilled 10 per cent phenylephrine into 100 hypertensive patients, only six developed elevations of blood pressure, all less than 10 torr. The same authors report finding no significant elevations of blood pressure in 20 patients who received topical phenylephrine following operations on eye muscles. However, none of these three studies was controlled, and in none were the precise doses of phenylephrine documented.

Even in view of the above studies, it seems likely that severe hypertension can occur after the topical application of 10 per cent phenylephrine ophthalmic solutions. Such hypertension would be especially dangerous in elderly patients, who would be more likely to suffer vascular accidents or pulmonary edema. In addition, marked hypertension postoperatively may promote intraocular hemorrhage in situations in which the eye has been opened during the operation. These systemic effects may be related in part to the total dose, as in the case of Patient 2, a 12-pound infant who received approximately 10 mg of phenylephrine. Systemic absorption may be enhanced in a diseased or post-surgical eye. Certain individuals may be more susceptible to the effects of the systemically absorbed drug. Finally, it is possible that the hypertensive effect may be caused by the combination of phenylephrine with some other drug, such as cyclopentolate. It is also not clear whether the main site of absorption is the conjunctiva or the nasal mucosa after drainage via the tear ducts.

Aviado has stated that the 10 per cent phenylephrine solution should not be used because of its potentially hazardous cardiovascular side-effects. It seems likely that these side-effects could be avoided by using a solution of lower concentration, as less drug would be available for absorption. A possible objection is that solutions of less than 10 per cent may not produce sufficient mydriasis to be clinically useful. However, Haddad et al. prepared a dose-response curve for phenylephrine using solutions ranging from 0.1 to 10 per cent, and they showed very little increase in mydriatic effect above a 5 per cent solution. The issue is somewhat clouded, however, in that they used freshly prepared aqueous solutions. The 10 per cent commercial preparation, which they also tested, produced only as much mydriasis as in the 2.25 per cent fresh solution. They suggested differences in pH, addition of preservatives to the commercial solution, and instability of the drug during storage as possible explanations for the disparity.

Anesthesiologists should be aware of the possibility of adverse reactions to phenylephrine administered topically, because they are likely to be called upon to treat them when they occur intraoperatively or in the immediate postoperative period. Until the situation is further elucidated, the use of incremental doses of chlorpromazine would seem to be a rational approach to the management of this complication. In cases of severe hypertension, a titrated intravenous infusion of trimethaphan (Arfonad) or phenotamine mesylate (Regitine) may be a useful alternative.

References