at one-minute intervals throughout the experiment. Minute volume was measured with a Bennett ventilation meter. In 3 patients the excitement stage was such that a small dose of thiopental was necessary to avoid displacement of the arterial cannula. At the end of a maximum period of five minutes, the flow rates were changed to 8 liters nitrous oxide per minute and 2 liters of oxygen. Studies of arterial oxygen saturation were terminated after three minutes at this flow rate.

After three minutes of breathing a high flow of oxygen by mask, the arterial oxygen saturation rose to above 100 per cent. For the first three minutes of low oxygen-high nitrous oxide flow, the arterial oxygen saturations gradually declined but remained above the resting level. At the end of four minutes the arterial oxygen saturation was below the resting state. At the end of five minutes the arterial blood was noted to be dark, although cyanosis was not definite in all patients. Upon changing to a flow of 8 liters per minute of nitrous oxide and 2 liters per minute of oxygen, the oxygen saturation rose toward the resting level. The minute volume determinations were unsatisfactory and were discontinued.

The resting level of arterial oxygen saturation in these patients, although below 95 per cent was considered normal and attributed to sedation. A low oxygen flow for three minutes did not materially affect the arterial oxygen saturation. After three minutes, however, two changes were noted: arterial oxygen saturation fell at a rapid rate, and there was a wide spread in the deviation from the mean. Thus three or three and one-half minutes is the limit of time that the patient may be continued on low oxygen-high nitrous oxide mixture and still maintain a relatively normal arterial oxygen saturation. Upon increasing the oxygen to 2 liters per minute while maintaining nitrous oxide at 8 liters per minute the oxygen saturations rise but do not reach the resting level.

We hope to repeat these experiments with a pneumotachograph and correlate the minute volume with the arterial oxygen saturations. We also want to measure the concentrations of nitrous-oxide and oxygen in the breathing bag that are actually being offered to these patients at serial points of the experiment.

The Effects of Caffeine, Codeine, Morphine and Combinations of Caffeine and Narcotics on the Respiratory Center. J. WELDON BELLVILLE, M.D., KUO CHEN WANG, M.D., STANLEY L. WALLENSTEIN, M.S., AND WILLIAM S. HOWLAND, M.D., the Division of Anesthesiology, Memorial Center for Cancer and Allied Diseases, New York City, New York.

IN order to study the respiratory effects of caffeine, codeine and morphine a double blind, factorial study was set up. A modification (Seed *et al.*, Arch. internat, pharmacodyn., in press) of the method of Eckenhoff (ANESTHESIOLOGY 17: 66, 1956) was employed to measure the respiratory response to increasing concentrations of endogenous carbon dioxide in man. Two control runs were obtained after which the subject received medication. Runs were obtained 1 and 2 hours after drug. The following medications were administered intramuscularly in a random order to each subject: placebo, caffeine 62.5 mg., caffeine 125 mg., caffeine 250 mg., codeine 60 mg., codeine 60 mg. plus caffeine 62.5 mg., codeine 60 mg. plus caffeine 125 mg., morphine 10 mg., morphine 10 mg. plus caffeine 62.5 mg., and morphine 10 mg. plus caffeine 125 mg. To avoid cumulative effects at least 36 hours elapsed between administration of medications. Alveolar ventilation—alveolar carbon dioxide tension response curves were plotted for both control runs and for 1 and 2 hours after medication. Displacement of the alveolar ventilation—alveolar carbon dioxide tension response curve to the right or left was then used to assay respiratory depression or stimulation respectively. Analysis of variance indicated that the variance due to treatment and subjects was significant ($P > 0.01$). Orthogonal treatment comparisons were made. Morphine produced significantly greater ($P > 0.05$) respiratory depression than codeine. Caffeine produced a significant ($P > 0.05$) decrease in the respiratory depression caused by morphine, but not in that

due to codeine. Caffeine alone in the doses used in this study was not significantly different from placebo. (Supported by a grant from Burroughs, Wellcome & Co., U. S. A., Inc.)

DISPLACEMENT OF RESPONSE CURVE IN MM. HG CARBON DIOXIDE TENSION

	Subject				Mean
	A	B	C	D	
Placebo	.65	2.25	1.4	−.75	.89
Morphine 10 mg.	6.35	15.9	9.05	7.5	9.7
Morphine 10 mg. + Caffeine 62.5 mg.	2.75	10.95	6.5	11.3	7.88
Morphine 10 mg. + Caffeine 125 mg.	3.9	7.1	4.25	5.7	5.24
Codeine 60 mg.	3.2	10.0	4.05	8.7	6.49
Codeine 60 mg. + Caffeine 62.5 mg.	1.35	9.3	5.7	7.35	5.93
Codeine 60 mg. + Caffeine 125 mg.	3.8	6.15	6.0	4.75	5.18
Caffeine 62.5 mg.	−.15	0	−.75	.15	−.19
Caffeine 125 mg.	−.6	2.8	0	−1.6	.15
Caffeine 250 mg.	−.25	2.5	2.8	−1.65	.85

Use of Intracarotid Arterial Procaine During Cranial Arteriography. WILLIAM F. BREHM, M.D., ARTHUR B. KING, M.D., JOHN B. COUGHLIN, M.D., AND JACK YOUNG, M.D., Departments of Anesthesiology and Neurosurgery of the Guthrie Clinic-Robert Packer Hospital, Sayre, Pennsylvania.

RADIOPAQUE contrast media injected into the carotid artery produces some degree of vasospasm, making visualization of cerebral vessels unsatisfactory. Attempts at prevention of spasm by the use of subcutaneous papaverine or by stellate block were unsatisfactory in our hands. To test the effect of intravascular procaine, which is known to release vasospasm, procaine was injected into the carotid arteries of 30 rabbits. We found that 15 mg./kg. could be injected without complications if the rabbits were protected with sleeping doses of pentobarbital. Following these preliminary observations a technique for injecting procaine into the carotid arteries of human patients has been evolved. The present report is on the use of the procedure in 100 patients during carotid cerebral aniography. Percutaneous carotid artery puncture was made through a local anesthetic skin wheal with the patient anesthetized with thiopental-nitrous oxide-oxygen. Ten cubic centimeters of 25 per cent Hypaque was then injected and the first of a stereopair of lateral radiographs was made. Two hundred milligrams of 1 per cent procaine was injected in about a 20-second period, and two minutes later a second radiograph was made with Hypaque.

Pulse and blood pressure remained unchanged in 73 patients and rose in 21 patients. Blood pressure decreased in six patients (the greatest decline was 40 mm. Hg). Sixty-eight patients showed no change in respiration to casual observation. Ten patients demonstrated hypopnea and 22 patients developed apnea within one and one-half minutes, lasting an average of one to three minutes. Respiration was easily assisted.

Ten patients demonstrated cortical irritation manifested by simple contralateral extremity spasticity to mild convulsive movements. The duration of the attacks was short and none was adjudged severe or harmful to the patient. All occurred in patients to whom less than 350 mg. of thiopental had been administered.

Dilatation of the retinal vessels was observed in all the 10 patients in which a retinal examination was made. Dilatation of the ipsilateral pupil occurred within 30 seconds from the start of the procaine injection when the needle was in position for Hypaque to enter the internal carotid artery. The dilated pupil test was correct for needle placement in 96 per cent of the cases. Shifting of the needle could explain three failures of the test and one patient had multiple arteriovenous fistulae.