Fifty patients were studied in the evaluation of the cholinergic effect. There were no marked cardiovascular changes. All patients showed a slight increase in heart rate. Vasodilatation, as measured by injection of sclera, was difficult to evaluate. A decrease in salivation was greatest in the oxyphenonium group. There was no difference in the incidence of side effects between these anticholingeric drugs.

One hundred patients were studied in the narcotic and narcotic antagonist group. The greatest reduction in blood pressure and respiratory minute volume occurred when meperidine without the antidote levallorphan was used. The sedative effect as indicated by drowsiness on arrival in operating room and reduction in thiopental induction dose was significantly greater with the combinations than with the placebo. The side effects were greatest in the placebo group.

This pilot study using the "double blind" method to evaluate premedication drugs has been undertaken in an attempt to find a way to best measure their effects. It is obvious that with random sampling of patients scatter graphs and statistical significance must be determined. Thus, this study is being used as a survey in preparation for a more extensive premedication study.

We learned the following from this study. A control group must be included in addition to the placebo group. The use of the respiratory minute volume to measure respiratory depression gives some scattered measurements that indicate that this measure may not be significant. The determination of this measurement under anesthesia and using CO_2 as a respiratory stimulus seems more accurate. The use of the amount of thiopental necessary to abolish the eyelash reflex in evaluating premedication sedation effect appears to be an accurate measurement.

Effect of Changes in Tidal Volume and Alveolar pCO_2 on Physiological Dead Space. D. Y. Cooper, M.D., and C. J. Lambertson, M.D., Dept. of Pharmacology and Harrison Dept. of Surgical Research, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Physiological dead space, calculated from measurements of arterial pCO_2, was previously reported to be markedly increased by carbon dioxide inhalation (Federation Proc. 12: 28, 1953). This investigation attempts to separate influences of tidal volume and alveolar pCO_2 upon dead space. Dead space changes, calculated from alveolar or arterial pCO_2 were determined during several levels of voluntary hyperventilation, exercise hyperventilation, and increase in tidal ventilation without alteration of alveolar pCO_2. Increase in tidal volume alone (Alv. pCO_2 39 mm. Hg) of one liter enlarged dead space 106 cc. With the same tidal volume change dead space increases were 100 cc. during exercise (Art. pCO_2 39 mm. Hg), 258 cc. during carbon dioxide breathing (Art. pCO_2 51 mm. Hg) and 56 cc. during voluntary hyperventilation (Alv. pCO_2 30 mm. Hg) with alveolar pCO_2 constant, dead space increased 11 cc./100 cc. increase in tidal volume. Deducting tidal volume effect from dead space in carbon dioxide breathing and voluntary hyperventilation indicated that, at constant tidal volume, hypercapnia enlarged dead space about 30 cc./mm. Hg increased in pCO_2; while hypocapnia diminished dead space about 3 cc./mm. Hg decrease in pCO_2. It is suggested that a pharmacodynamic effect of altered pCO_2 is normally algebraically additive with a separate, mechanical effect upon dead space of altered tidal volume.

The Effect of Gaseous Anesthetic Agents on Evoked Central Nervous System Responses. Hamilton S. Davis, M.D., William F. Collins, M.D., Clark T. Randt, M.D., and William H. Dillon, M.D., The Department of Surgery (Divisions of Anesthesiology and Neurosurgery) and the Department of Medicine (Division of Neurology), Western Reserve University School of Medicine, Cleveland, Ohio.

With the demonstration by French, Verzeano and Magoun [Arch. Neurol. Psychiat. 69: 519–529, 1953], of depression of reticular formation activity by ether and pentobarbital, an area of the central nervous system which had previously been found to influence the level of consciousness in animals and man was shown to be sensitive to anesthetic agents.

The multisynaptic structure of the reticular system was demonstrated by Maruzzi and Magoun [Electroenceph. Clin. Neurophysiol. 1: 455–473, 1949]. The depression of synaptic transmission by anesthetic agents was shown by Larrabee and Posternak [J. Neurophysiol. 15: 91–114, 1952].

The present study with gaseous agents is one of a series designed to document the effects of various anesthetic and related drugs on the oligosynaptic lemniscothalamic system and multisynaptic midbrain reticular system of the cat. Cyclopropane 40 per cent, ethylene 77 per cent, and nitrous oxide 77 per cent were studied, the diluent being oxygen in all cases.

Sixteen cats comprised this series. Each cat was prepared using cyclopropane anesthesia, immobilized with muscle relaxants, respired artificially and the central anesthetic effects withdrawn. Using electrical stimulation of the superficial radial nerve, evoked responses in the posteroventrolateral nucleus of the thalamus and midbrain reticular formation were recorded by means of a cathode ray oscilloscope. After control periods, in which constancy of the responses was demonstrated, the gases were given and the effects on the evoked potentials recorded photographically.

It was found that the oligosynaptic thalamic spike potential was minimally affected by these gases, while the multisynaptic midbrain reticular formation wave potential was invariably depressed by all three. This effect was most striking with cyclopropane, with which the potential was promptly obliterated, less with ethylene and least with nitrous oxide. There was no change in the conduction latency of either potential, which adds support to previous observations that synapses, rather than axons, are primarily affected by anesthetic agents. Hypoxia, hypotension, hypercarbia and hypothermia were carefully prevented in all experiments.

The results indicate a high degree of sensitivity of the midbrain reticular formation to the effects of the gaseous anesthetic agents and suggest that this may be a useful experimental tool in the evaluation of anesthetic agents in general.

Cardiovascular Studies on Muscle Relaxants. J. D. Elder, M.D., H. Johnson, M.D., and L. S. Binder, M.D., State University of New York, College of Medicine, New York, New York.

The effects of curare on the cardiovascular system have been observed under thiopental nitrous oxide and oxygen anesthesia in ten hospital patients. The modalities observed were arterial blood pressure (mean), central venous pressure, cardiac output and the electrocardiograph (Lead II). With single doses of 12 to 24 mg. of *d*-tubocurarine the averages of the cardiac index, arterial blood pressure, venous pressure and cardiac work show decreases which were too small to have statistical significance. The total peripheral resistance and pulse rates showed even smaller increases.

Since there were no significant changes in the mean values, an attempt was made to correlate individual shifts with doses given, the age, or the condition of the patient. No such relationship can be demonstrated.

In exactly the same manner the above measurements have been made on six patients to whom succinylcholine chloride in doses of 20 to 60 mg. were administered. The averages for this group showed changes in the neighborhood of 5 per cent, and could easily have been due to inherent variation of measurement in all instances.

Within the scope of this study to date the direct cardiovascular depressant effect of the muscle relaxant drugs has not been great enough to assume statistical significance.

Laboratory Investigation of a New "Universal Analeptic" (WIN 7969). L. W. Fabian, M.D., M. Bourgeois-Gavardin, M.D., and C. R. Stephen, M.D., Department of Anesthesiology, Duke University School of Medicine, Durham, North Carolina.

In basic studies, WIN 7969 (N-N′ dibutylethylene diamine dicarboxy bismorpholide) has demonstrated greater potency than either nikethamide or pentylenetetrazole (metrazol®) in the treatment of opiate or barbiturate depression with a wider margin of safety