

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 lemnisothalamic 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cyclopropane anesthesia, immobilized with muscle relaxants, respired artificially and the central anesthetic effects withdrawn.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

than these two analeptics. Convulsant activity was not evident in animals until ten times the therapeutic dose was administered. These advantages have stimulated a study of WIN 7969 to ascertain its value in the therapy of prolonged postanesthetic depression.

Dogs were used as experimental animals. Observations were made by simultaneously recording the electrocardiogram, electroencephalogram, arterial blood pressure, and pneumotachogram. Anesthesia for endotracheal intubation and preparation of the animal was with thiamylal. The same barbiturate was used in studying the analeptic properties of WIN 7969. Control observations were made in 6 dogs following the intravenous injection of 2 per cent thiamylal solution (20 mg./Kg.). The degree of depression and the time required for spontaneous recovery was noted. An active cough reflex served as the end point for the control study. Immediately after this reflex was noted, a second injection of thiamylal (20 mg./Kg.) was given, followed in 5 minutes by WIN 7969 (4 mg./Kg.). Comparisons of the control and test records were made. WIN 7969 produced an immediate rise in arterial blood pressure, pulse pressure, respiratory minute volume, respiratory rate, and initiated a variety of cardiac arrhythmias. These phenomena were believed to represent an adrenergic effect, since benzodioxan (2 mg./Kg.), regitine (0.5 mg./Kg.), and chlorpromazine (2.5 mg./Kg.) were all able to prevent or reverse the hypertension and cardiac arrhythmias. Hexamethonium and Arfonad® failed to block such responses. Twenty minutes following the barbiturate injections, there was an average increase of 160 per cent in respiratory rate, an 85 per cent increase in mean arterial pressure, and a 45 per cent decrease in heart rate. Recovery from the depressant effects of the barbiturate occurred in approximately one-half the time required for the control.

A comparative study using WIN 7969 (4 mg./Kg.), nikethamide (25 mg./Kg.) and pentylenetetrazole (5 mg./Kg.) was performed on a series of 7 dogs under similar circumstances. Usually, an interval of at least 30 minutes was allowed between drug injections. Comparing average maximal response of the three drugs in antagonizing the barbiturate depression, WIN 7969 increased respiratory rate 45 per cent, nikethamide 25 per cent, and pentylenetetrazole 35 per cent. The effect upon blood pressure was a 120 per cent, 68 per cent, and 24 per cent increase respectively. In two experiments, where pentylenetetrazole failed to increase or initiate respiratory activity, WIN 7969 was able to do so.

WIN 7969 (4 mg./Kg.) effectively reversed respiratory and cardiovascular depression produced in 4 animals by the injection of morphine (5 mg./Kg.).

Our investigations to date have indicated that WIN 7969 may prove to be of value. However, further assessment of the drug must be made, particularly in regard to the cardiac irritability produced by the drug. We are currently investigating the combination of thiamylal and WIN 7969 in order to produce hypnosis and sedation without cardiorespiratory depression.

Röntgen Ray Studies of Airway Problems; I. The Oropharyngeal Airway

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THE object of this study was to correlate the anatomy of supralaryngeal obstruction with the occasional failure of oral airways to relieve the obstruction. Lateral roentgen rays are used to observe the effects of posture and of various airways on the configuration of the pharynx.

The normal waking air passage is narrowest behind the soft palate and at the entrance to the larynx. The base of the tongue is some distance in front of the posterior pharyngeal wall, being held forward by muscular attachments to the mandible and hyoid bone. When the tone of these muscles is lost at the onset of general anesthesia, the tongue falls back, accompanied by the epiglottis. Since this cartilage also forms the anterior wall of the laryngeal entrance, the collapse of the tongue involves a partial collapse of the laryngeal aditus as well.