trations were administered ranging from 5 to 40 per cent. A nonrebreathing system with mechanical hyperventilation was used. Carbon dioxide 3–4 per cent was added to maintain control CO_2 levels. *Results:* Neuromuscular block in the presence of muscle twitch potentiation was suggested by the divergence of dose-response curves for non-curarized and curarized cat soleus and gastrocnemius. Curarized direct preparations were potentiated more by cyclopropane than were indirect preparations, suggesting that some degree of neuromuscular block existed in the latter. Motor nerve terminal activity as measured by post-tetanic repetitive activity showed uniform depression of the prejunctional element. This was interpreted as evidence for incipient neuromuscular block. Post-tetanic potentiation, a consequence of motor nerve terminal repetition in cat soleus, was depressed or abolished by cyclopropane. In cat gastrocnemius, however, where post-tetanic potentiation is generated within the muscle and not by nerve terminal repetition, cyclopropane prolongs the duration of post-tetanic potentiation. The degree of potentiation is greater in gastrocnemius muscle than in soleus for both curarized and non-curarized preparations. In frog sartorius (as distinct from cat preparations) neuromuscular block rather than muscle potentiation is the predominant effect; muscle potentiation is prominent only in the curarized direct twitch. *Conclusions:* Through the examination of different muscles and different species, marked and varied effects of cyclopropane on the neuromuscular complex become evident. In clinical practice, the inability of ordinary doses of cyclopropane to produce profound muscle relaxation may be related to potentiation of muscle; with higher doses, even though muscle becomes more sensitized, profound relaxation can be secured because nerve impulses are blocked from muscle at either central synapses or the neuromuscular junction.

The Effect of Vagolytic Drugs on Ventricular Arrythmias During Cyclopropane Anesthesia. LEONARD F. WALTS, M.D., and WILLIAM MCFARLAND, M.D., *University of California, Los Angeles, School of Medicine, Department of Surgery/Anesthesiology, Los Angeles, California.* Atropine given intravenously during cyclopropane anesthesia produced severe disturbances in ventricular rhythm in 52 per cent of patients tested (Jones, R. E., Deutsch, S., and Turndorf, H.: ANESTHESIOLOGY 22: 67, 1961). Walts and Prescott in an unpublished study found that gallamine, which has as a side effect cardiac vagolysis, produced similar disturbances in 56 per cent of patients tested. In the latter study, the authors observed that a second dose of gallamine, given after a return to normal sinus rhythm, failed to produce further abnormality in rhythm. This suggested the possibility that the first administration of gallamine afforded protection against the subsequent dose. *Method:* Healthy adult patients were divided into 2 groups. In group 1, 25 patients were given atropine or scopolamine, 0.3 to 0.4 mg. intramuscularly, with premedication. They received 0.6 mg. of atropine intravenously prior to the induction of anesthesia. Following induction with a thiobarbiturate and tracheal intubation, facilitated by using succinylcholine chloride, anesthesia was maintained with cyclopropane and oxygen. Respiration was controlled with a ventilator set to deliver a tidal volume 10 per cent in excess of predicted normal volume calculated from the Radford nomogram. After approximately 15 minutes, 100 mg. of gallamine were injected intravenously. In group 2, the regimen of the 25 patients differed in that they received 1.2 mg. of atropine prior to the induction of anesthesia and were challenged with 0.4 mg. of atropine rather than gallamine after approximately 15 minutes of cyclopropane and oxygen anesthesia. Changes in ECG, pulse, and blood pressure as a result of the atropine or gallamine challenge were noted and end-tidal P_{CO_2} was measured in 5 patients. *Results:* All patients were in a moderate depth of anesthesia (EEG levels 2 to 4). End-tidal P_{CO_2} was less than 40 mm. of mercury in all measured cases. In group 1, following the gallamine, only 3 patients (12 per cent) developed ventricular arrhythmias. In group 2, 3 patients (12 per cent) developed disturbances in ventricular rhythm in response to the atropine. *Comment:* It has long been known that increased sympathetic tone during cyclopropane anesthesia precipitates ventricular arrhythmias. The autonomic imbalance can be

produced by an injection of epinephrine or result from the endogenous release of catecholamines in hypercarbia. It is now clear that cardiac arrhythmias are produced, not only by an augmented sympathetic tone, but also by a reduction in parasympathetic tone. Thus, atropine or gallamine produced disturbances similar to those caused by epinephrine. It remains to be determined whether the mechanism of action under both circumstances is the same. In the past literature, it has been noted that hypercarbia afforded protection against epinephrine-induced arrhythmias in the dog anesthetized with cyclopropane. Ueda and associates demonstrated that protection is due to catecholamine tachyphylaxis (ANESTHESIOLOGY 23: 342, 1962). In our study we have demonstrated that atropine will protect the heart against subsequent injections of vagolytic drugs. We were able to reduce the incidence of arrhythmia from greater than 50 per cent to 12 per cent by giving atropine prior to induction of anesthesia. If the mechanism of production of arrhythmia by atropine is, in fact, unopposed catecholamine acting on the sensitized myocardium, the explanation for the protection afforded by the initial dose of intravenous atropine might be, similarly, catecholamine tachyphylaxis.

The Doxapram Test: A New Technique for the Differential Diagnosis of Apnea. ALON P. WINNIE, M.D., and VINCENT J. COLLINS, M.D., *Department of Anesthesiology, Cook County Hospital, Hektoen Institute for Medical Research, and Northwestern University School of Medicine, Chicago, Illinois.* In spite of continuing advances in the field of anesthesia, the failure of a patient to resume spontaneous respirations at the completion of operation remains a vexing problem. Because of the practice of combining barbiturates, narcotics, inhalation anesthetics and muscle relaxants during the course of an anesthetic, it is sometimes exceedingly difficult to identify the agent responsible for apnea. It would be of great practical value to have a means of determining whether or not the apnea is due to central depression or peripheral neuromuscular blockade. The present paper reports the development of such a test. *Methods and Results:* In studies to be reported elsewhere the authors demonstrated that doxapram hydrochloride *selectively* stimulated the depressed respiratory center regardless of type or degree of depression, as long as there was adequate cerebral blood flow. The standard response to doxapram in patients whose respiratory centers were depressed with an average of 14 mg./kg. of thiopental was as follows: one arm-to-brain circulation time after intravenous injection there was a profound increase in ventilation consisting of a 360 ml. average increase in tidal volume and an average increase in respiratory rate of 6 breaths per minute. Although the period of intense hyperventilation persisted for only 3 to 4 minutes, ventilation remained elevated above preinjection levels for over 30 minutes. Because of this ability of doxapram to selectively stimulate even the depressed respiratory center, we have used it as a diagnostic tool in the differential diagnosis of postanesthetic apnea. Over the past two years the doxapram test has been used in over 30 patients who remained apneic more than 15 minutes after the discontinuance of anesthesia, and in every case the mechanism involved became immediately evident. If 2 mg./kg. of the drug evoked the respiratory response described above, then the cause of the apnea was central depression. If there was no response, the cause was persistent neuromuscular block. In the patient who was breathing postoperatively but with an inadequate tidal volume, the *doxapram test* served as an intermediate step in distinguishing residual central depression from partial curarization. If the cause of the hypoventilation was simply central depression there was the typical respiratory response to doxapram, namely, an increase in both respiratory rate and tidal volume. However, if the cause was persistent partial curarization, the response was somewhat different: there was still an increase in respiratory rate but a *decrease* in tidal volume. This is due to the fact that the partly curarized respiratory muscles were already responding with a maximal volume, so the stimulated respiratory center can only respond with an increase in rate. This in turn resulted in a decrease in tidal volume. *Conclusion:* As a result of our experience we believe that the *doxapram test* is a valuable