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

tool in the differential diagnosis of apnea, and that it is much simpler to accomplish than the ulnar nerve stimulation test advocated by Churchill-Davidson (Churchill-Davidson, H. C.: Canad. Anaesth. Soc. J. 8: 91, 1961). In addition, it is frequently of therapeutic as well as diagnostic value, for in the vast majority of cases where the apnea is of central origin, doxapram results in the reinstitution of spontaneous respiration and in the almost immediate arousal of the patient.

Hemodynamics During Neurolept Analgesia. HOWARD L. ZAUDER, M.D., PH.D., LOUIS R. M. DEL GUERCIO, M.D., NEIL FEINS, M.D., NEIL BARTON, M.D., and STEWART WOLLMAN, M.D., *Departments of Anesthesiology and Surgery, Albert Einstein College of Medicine, New York City.* A hallmark of neurolept analgesia as produced by nitrous oxide-oxygen supplemented with a 50:1 mixture of droperidol (1 mg./ml.) and fentanyl (0.02 mg./ml.) is the stability of the cardiovascular system as monitored clinically. Direct measurement of cardiac output and related hemodynamic parameters are required to properly assess the action of this combination of drugs on the circulation. *Methods:* Twenty-two observations were carried out, prior to major surgery, in 9 geriatric patients. The average age was 69, the range extending from 46 to 94 years. Sixty to ninety minutes prior to study, 0.4 mg. of atropine was administered intramuscularly. All cannulations were performed on the night prior to study. Cardiac output, central venous pressure, mean circulation time, systolic, diastolic and mean blood pressure and pulse rate were determined by standard techniques. Arterial and venous P_{O_2}, P_{CO_2} and *p*H were determined with the appropriate electrode. From the data stroke index, total peripheral resistance, stroke work, mean ejection rate, central blood volume and buffer base were calculated. Following the control studies 2–14 ml. of droperidol-fentanyl were given rapidly intravenously. Within 3–4 minutes N_2O–O_2 in a 50:50 mixture (7–9 liters total flow) was administered by mask. Determinations of the cardiorespiratory parameters were made 15 minutes later. In 4 patients these were repeated 15 minutes later. The cardiac index rose from 3.15 ± 0.32 * liters/minute/m.^{2} to 3.36 ± 0.18 * liters/minute/m.^{2}. The stroke index was constant, 42.2 ± 2.4 * ml./m.^{2} before and 42.7 ± 5.4 * ml./m.^{2} after drug administration. Stroke work was likewise unchanged, amounting to 81.9 ± 10 * gram meters before and 80.9 ± 10 * gram meters during anesthesia. The mean ejection rate rose from 123 ± 10 * ml./systolic second/m.^{2} to 138 ± 10 * ml./systolic second/m.^{2}. Total peripheral resistance, on the other hand, fell from 1545 ± 131 * dynes/second/cm.$^{-5}$ to 1265 ± 299 * dynes/second/cm.$^{-5}$. The mean circulation varied little, from 17.4 ± 1.9 * seconds before to 16.0 ± 1.2 * seconds after drug administration. The central venous pressure rose from 7.1 ± 3.3 * cm. of water to 9.6 ± 3.0 * cm. of water. While the mean blood pressure fell from 97.6 ± 1.5 * mm. of mercury to 87.4 ± 2.0 * mm. of mercury. Central blood volume declined as did the pulse rate, the former from 1.49 ± 0.05 * liters to 1.47 ± 0.17 * liters, the latter from 81.3 ± 5.5 * to 75.6 ± 3.7 *. Arterial P_{CO_2} rose from 36.1 ± 1.0 mm. of mercury to 41.2 ± 2.2 * mm. of mercury, this was reflected in the *p*H which fell from 7.43 ± 0.04 to 7.40 ± 0.04. Buffer base was unchanged from the central value of 50.0 ± 1.9 * mEq./liter. When scrutinized by the paired *t* test only the fall in blood pressure is statistically significant ($P = 0.1$). *Conclusion:* From these results it is concluded that neurolept analgesia as produced in these patients is without significant effect on the cardiovascular system of the unstressed surgical patient.

* Standard error of the mean.

Effect of pH on Activity of Topical Anesthetics. RICHARD ZEPERNICK, M.D., EDWIN HYDE, M.D., and JOHN ADRIANI, M.D., *Department of Anesthesiology, Charity Hospital, New Orleans, Louisiana.* In a recent study comparing the activity and potency of topical anesthetics, we observed that the maximum duration of anesthesia topically was obtained by using solutions of the salt of the drug whose *p*H ranged from 6.2 to 6.9. It is often stated that alkalinization of solutions enhances their activity. In view of the fact that our findings are not in agreement with accepted thinking and that we did not study this aspect