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

of the problem in detail, we are pursuing our studies further. *Method:* Our studies were done in man using the technique described in previous reports (Clin. Pharmacol. Ther. 5: 49, 1964), in which an electrical current was used to stimulate the tip of the tongue. Solutions were prepared using phosphates as buffers. *Results:* The duration and intensity of action was shortened when the *p*H of the solution was less than 6.1 or greater than 6.9 following application of 1 per cent tetracaine, 4 per cent cocaine, 5 per cent piperocaine, 5 per cent hexylcaine, 10 per cent procaine and 1 per cent dyclonine. The decrease in duration was not striking when the *p*H of 7 was exceeded until the drug began to precipitate, after which there was a marked decrease. Exceeding the maximum effective concentration of the salt of a drug shortens the duration and prolongs the latent period. The increase in total acid in concentrated solutions of the salt interferes with the buffering capacity of the tissues and accounts for the loss of activity. Pretreatment of the tip of the tongue with 1 per cent acetic acid, after which 4 per cent cocaine hydrochloride was applied, shortened the duration of action. Additional data on the alkalinization were obtained (1) by pretreating the mucous surface with 5 per cent sodium bicarbonate 5 minutes before the drug was applied and (2) by adding sodium bicarbonate directly to a solution of the salt until slight clouding due to precipitation of the free base appeared, after which the solution was applied to the surface. The period of latency and the overall duration were both shorter than those observed when the salts were used with tetracaine, cocaine, procaine and dyclonine. Increasing the concentration of a drug applied to a previously alkalinized surface caused a decrease in the period of latency and an increase in intensity. Larger voltages were required to re-elicit the response at the tongue. The subject described the feeling of numbness as being more intense. The supernatant solution of cocaine base (a saturated solution) produced a feeble response. Duration of anesthesia averaged less than five minutes. Such a solution is highly dilute compared to that of the salt. (Solubility 1 g. in 600 ml. of water 25° C. versus 1 g. in 0.4 ml.) When 2 per cent tetracaine (twice the maximum effective concentration) was applied to a pre-alkalinized surface to reduce the quantity of acid, the duration was the same as that of a 1 per cent alkalinized solution. A suspension resulting from alkalinization of a mixture of 20 per cent cocaine or 1 per cent tetracaine produced the same duration of anesthesia as the solution alkalinized to the point of turbidity. Alkalinization did not influence the duration, period of latency or effectiveness of non-nitrogenous hydroxy compounds, such as phenol, menthol and benzyl alcohol. Dyclonine (Dyclone), a propiophenone intermediate between the alcohol type and the classical nitrogen type, was also studied in detail since this drug is relatively free of systemic effects. The ½ per cent solution which is the commercially available preparation is not nearly as effective as the 1 per cent solution which appears to be the maximum effective concentration. Increasing the concentration to 2½ per cent did not prolong the duration on the tip of the tongue. At a *p*H of 7.5 the latent period was 1.4 minutes; the duration 15.5 minutes. At a *p*H of 6.7 the period of latency was 2.1 minutes and the duration was 25 minutes. At a *p*H of 6.4 the period of latency was 2.4 minutes and the duration was 28.1 minutes. At a *p*H of 5.5 the latent period was 3.5 minutes and the duration 22.2 minutes. *Conclusion:* It appears from our studies that *p*H plays an important role in the establishment of topical anesthesia and that alkalinization of solutions does not extend the duration of anesthesia.