

Abstracts

Work in Progress

John Adriani, M.D., Editor

The following are abstracts of papers presented at the WORK IN PROGRESS program of the Annual Meeting of The American Society of Anesthesiologists, New York, October 23, 24, 25, and 26, 1962.

Comparative Potency and Duration of Action of Topical Anesthetic Drugs in Man.

JOHN ADRIANI, M.D., and RICHARD ZEPERNICK, M. D., *Department of Anesthesia, Charity Hospital, and Department of Surgery, Louisiana State University School of Medicine, New Orleans, Louisiana.* Comparative data on the efficacy of topical anesthetics in man are meagre. Findings in animal experiments and those of clinical experience do not often agree. *Method:* We obtained comparative data in man using a pulsatile direct-electrical current, ranging between 0.2 and 2 volts, applied at the tip of the tongue, conjunctival sac, and other areas covered by mucous membranes. The abolition of a tingling sensation coincided with the disappearance of the pin prick and other painful stimuli. Obtundation was partial with some drugs and complete with others. Variations in voltage were an index of potency. *Results:* An optimum concentration existed for each topically-applied drug. Duration of action increased as the concentration increased until a maximal optimal concentration was reached. The period of latency was shortened as the maximal effective concentration was approached. The period of latency for 4 per cent cocaine was 4 minutes; the duration 10.2 minutes. At 10 per cent the latent period was 3.2 minutes; the duration 31.5 minutes—while with 20 per cent cocaine, the period of latency was 30 seconds and the duration 54 minutes. Similar findings were observed for other commonly-used drugs. In order of duration at maximal effective concentration were tetracaine 1 per cent—55 minutes; cocaine 15 per cent—54 minutes; dibucaine 0.5 per cent—46

minutes; dyclonine 1 per cent—26 minutes; lidocaine 4 per cent—15 minutes; hexylcaine 7.5 per cent—11 minutes; procaine 20 per cent—9 minutes; butacaine 20 per cent—9 minutes; piperocaine 5 per cent—8 minutes; mepivacaine 15 per cent—8 minutes; praxamine 2 per cent—8 minutes; pyribenzamine 4 per cent—8 minutes; benzocaine 20 per cent—4 minutes; mephanesin powder—3 minutes; benzyl alcohol 100 per cent—3 minutes, and menthol 3.5 per cent—1.5 minutes. Potency and duration of the block did not always parallel each other. Once the block was established, increasing the voltage again caused a response, although the response was feeble. Using this technique, lidocaine was the most potent agent. Next in order were tetracaine, dibucaine, cocaine, dyclonine, hexylcaine, piperocaine, butacaine, mepivacaine, pyribenzamine, benzocaine, mephanesin and benzyl alcohol. Chlorethone and bromsalizol were without effect. The effects of alkalization were studied by applying 5 per cent sodium bicarbonate to the tongue after which the salt of the local anesthetic was applied and by adding alkali directly to the solution of the salt until the free base precipitated. Clinically, procaine hydrochloride was ineffective topically. A progressive increase in concentration with prior alkalization produced a progressive shortening of the latent period and prolongation of the block with cocaine, tetracaine, and dyclonine. With procaine the latent period was shortened but the duration was lengthened. The intensity of the blockade was greater with alkalinized compounds than with solutions of the hydrochloride. Somewhat longer periods of latency

and duration of action were obtained by the preliminary alkalization of the tongue prior to application of the drug than when using the alkaline suspension. Vasoconstrictors allegedly retard absorption of the local anesthetic drug and prolong its effect. This is true intrathecally and perineurally but not topically. Neither norepinephrine, epinephrine, or ephedrine exerted any significant effect on the duration of the block. Angiotensin (Hypertensin) and vasopressin exert their effects by direct action on the smooth muscle and not on the adrenergic receptors. These were also studied in view of these differences in behavior. They exerted no significant prolonging effect on the block when mixed with cocaine and tetracaine. Hyaluronidase and demulcents caused no change.

The addition of various cations to solutions of local anesthetics allegedly prolongs the block. Calcium, potassium, sodium, magnesium and ammonium ions did not prolong the block of either tetracaine or cocaine when used in concentrations up to 5 per cent. No significant prolongation of action occurred when two local anesthetics at their optimal concentrations were mixed. A mixture of 15 per cent cocaine and 1 per cent tetracaine produced no greater duration of the block or period of latency than either of these drugs used alone.

Halothane and Cardiac Work. MILTON H. ALPER, M.D., and WERNER FLACKE, M.D., *Division of Anesthesia, Peter Bent Brigham Hospital, and Department of Pharmacology, Harvard Medical School, Boston, Massachusetts.* The administration of halothane in concentrations of 0.5 per cent or higher in the inspired gas significantly depresses myocardial contractility in the heart-lung preparation of the dog (Flacke, W., and Alper, M. H., *ANESTHESIOLOGY* 23: 793, 1962). The depression is manifested by a rise in right and left atrial pressures and a fall in systemic cardiac output at a constant height of the venous reservoir. *Method:* In the present experiments, this observation was extended to study the influence, if any, of the type of load imposed upon the heart. In the heart-lung preparation, systemic cardiac output and arterial resistance can be altered independently.

Cardiac output was increased by raising the venous reservoir in measured steps. Arterial pressure was varied by adjusting the setting of the Starling resistance. Halothane was administered from a Fluotec vaporizer. Determination of halothane concentrations in blood by gas chromatography showed that, at constant inspired concentration, about 90 per cent of the steady-state concentration was reached within ten minutes. It was found that, under halothane, an increased cardiac output was accompanied by a much smaller rise in left atrial pressure than with increased arterial pressure. In order to study this difference quantitatively, cardiac work was calculated as the product of systemic output and arterial pressure under conditions of increased output ("volume work") or increased pressure ("pressure work"). Ventricular function curves (Sarnoff, S. J., and Berglund, E.: *Circulation* 9: 706, 1954) were constructed by plotting left ventricular work against filling pressure, either measured directly by intraventricular catheter or approximated from left atrial pressure. *Results:* In control experiments, the ventricular function curves for "volume work" and for "pressure work" were not significantly different. After administration of 0.5 per cent halothane for at least 15 minutes, the curve resulting from increase in output was displaced in the direction of increased filling pressure, but the slope of the curve paralleled that of the control curve. The same maximal work could be obtained although at greater filling pressure. In contrast, the function curve resulting from increase in arterial pressure was not only displaced farther in the direction of increased filling pressure but also its slope was strikingly reduced. The maximum work obtainable at any filling pressure was greatly lowered. Recovery from the effect of halothane, measured 15 to 20 minutes after discontinuation of the anesthetic, was more complete with regard to "volume work" than with regard to "pressure work." Finally, infusion of *l*-norepinephrine at a rate of 1 to 3 μ g/minute enables the heart, under halothane, to increase its output with normal filling pressures; it did not restore completely the ability of the heart to work against a high resistance. *Conclusion:* It can be concluded that the depression of contractility by halothane com-