rectly proportional to the amount of chlorides. Blood serum, cerebrospinal fluid, and water are, within narrow limits, similar in this respect. (2) The determination of the bromide content by the Walter method in chloride-free fluid is reliable, the margin of error being quite limited. (3) Blood and cerebrospinal fluid containing similar quantities of chlorides would be liable to the same error, and the bromide contents obtained would be reliable for purposes of comparison. (4) For absolute reliability the technique of the Walter method should be modified as follows: *a.* The blood should be diluted with a NaCl solution, the strength of which is equal to that of the blood. *b.* The chloride contents of the blood and cerebrospinal fluid should be determined, and in computing the actual amount of bromides allowances should be made for the loss due to the chlorides. The present investigation shows that the loss caused by 0.6% NaCl (which is the average NaCl concentration in blood serum) is about 27%. Further studies are being made to determine the exact losses due to NaCl concentrations ranging from 0.4% to 0.9%.

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A Modified Class Demonstration of Difference Between Ephedrine and Epinephrine Blood-Pressure Response After Cocaine.

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The demonstration of cocaine sensitization for epinephrine and desensitization for ephedrine according to Sollmann and Hanzlik[1] calls for the following sequence of administration in a doubly vagotomized dog under barbital anesthesia: Epinephrine (0.05 mg. per kg.), ephedrine (2.5 mg. per kg., both intravenously), cocaine (10 mg. per kg., hypodermically), then repetition of the epinephrine and ephedrine injections after suitable intervals of time.

The epinephrine dosage should be 10 times less[1] and even as low as 0.002 mg. is very satisfactory in atropinized dogs under amytal anesthesia.

In regard to the ephedrine desensitization by cocaine we ran 3

[1] Sollmann, T., and Hanzlik, P. J., Experimental Pharmacology, W. B. Saunders, 1928, 227, 282.

experiments, each with a proper control without cocaine, using the same procedure as above, but only 2 mg. of ephedrine per kg. In 2 of these pairs of experiments we could not tell any difference between the cocaine and the control experiment; the second ephedrine dose was given one hour after the first in all cases. Also, in another study involving 30 dogs with even sex distribution and graded sizes, the average second ephedrine blood-pressure rise in terms of percentage of the first ephedrine rise was 53.3 with a standard deviation of 9.5 when ephedrine was followed by ephedrine, whereas the values for another 30 dogs was 40.0, standard deviation 11.4, when we gave ephedrine, cocaine and ephedrine. Thus, although the average is 25% lower when cocaine is given, the variability in response is so great that in many cases the ephedrine desensitization to itself would give values about the same as those obtained after ephedrine and cocaine, and in some cases would give even higher values than in the control experiment.

That cocaine sensitizes to epinephrine and depresses the ephedrine response may be demonstrated to a class more clearly as follows, using atropinized dogs, anesthetized with amytal.

(1) 0.02 cc. of 5% (1 mg.) cocaine per kg. injected intravenously, using 10 to 15 seconds, is shown to give but a very slight modification of the blood pressure (Fig. 1, A). Preliminary experiments have shown that this dose intravenously sensitizes to epinephrine; no attempt has been made to ascertain the minimum sensitizing intravenous dose of cocaine. We have purposely used a very small volume of cocaine solution of high concentration.

(2) 0.1 cc. of 1/33,300 epinephrine (0.003 mg.) per kg. is injected intravenously into a dog to show the normal response. A few minutes after the blood pressure has again become normal a similar dose of epinephrine is administered, and just when the initial rise has reached its maximum, 1 mg. of cocaine per kg. is injected intravenously. Any beginning fall is checked, and a moderate, somewhat prolonged rise occurs, showing the sensitization (Fig. 1, B1 and B2). The tracings show that unless the cocaine is given at just the right time (perhaps even better just before the maximum initial rise has been reached), the effect will be much less pronounced, due to the rapid destruction of the epinephrine. One may also show the full sensitization by injecting epinephrine a third time about 10 minutes later.

(3) By another tracing the typical prolonged response after intravenous injection of 0.1 cc. of 2% ephedrine (2 mg.) per kg. is demonstrated (Fig. 2, C).

Medium sized atropinized dogs, both sexes; amytal anesthesia. Time intervals, 1 minute.

COC, 0.02 cc. of 5% cocaine hydrochloride (1 mg.) per kg., intravenously.

ADR, 0.1 cc. of 1/33,300 epinephrine (adrenaline) hydrochloride (0.003 mg.) per kg., intravenously.

EPH, 0.1 cc. of 2% ephedrine hydrochloride (2 mg.) per kg., intravenously.

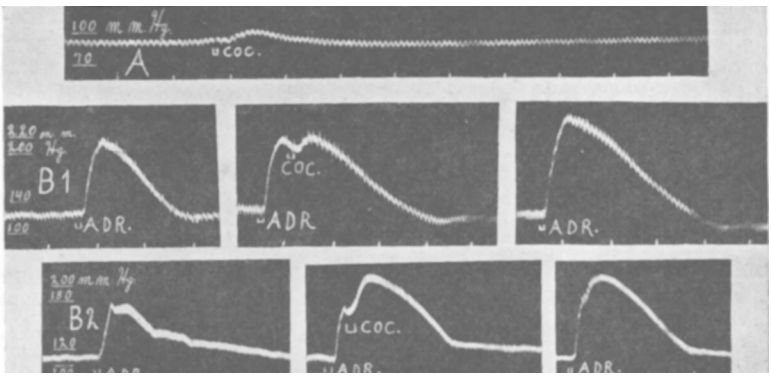

FIG. 1.

A. Effect of cocaine upon normal blood pressure.

B1 and B2. Normal epinephrine blood pressure rise. Sensitization of this response by injecting cocaine at the height of the initial rise of blood pressure. Epinephrine response after some minutes. Intervals between tracings represent about 6 minutes each.

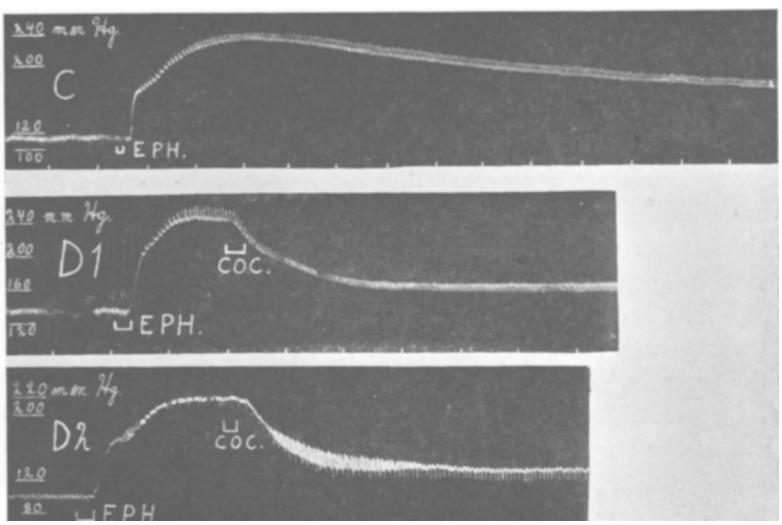

FIG. 2.

C. Effect of ephedrine upon normal blood pressure.

D1 and D2. Depression in the ephedrine response by injecting cocaine just after the maximum has been reached.

(4) Into a second dog a similar dose of ephedrine is injected intravenously. Shortly after the maximum response has been secured—2 to 3 minutes after the injection—1 mg. of cocaine per kg. is administered intravenously. There should be a sharp break in the curve, and blood pressure should reach a constant level in about 5 to 7 minutes (Fig. 2, D1 and D2). Although in these 2 tracings a constant level is reached a little above normal blood pressure, we have 2 other tracings in which it fell to normal, though not below it.

These 2 demonstrations show that upon intravenous injections of small doses of cocaine the epinephrine sensitization and the ephedrine desensitization occur almost immediately. According to Trendelenburg[2] the beneficial effect of cocaine and other local anesthetics upon the epinephrine response may in part be due to the slowing of circulation by such substances, "so that the epinephrine reaches the arterioles in concentrated solution." Our tracing B2 shows that the sensitization takes place just as well when the epinephrine is already in the arterioles.

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Microincineration of Tubercles.

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The technic of microincineration as developed by Policard[1] and modified by Scott[2] has been used in studying the mineral content of tubercles from human tuberculosis and experimental tuberculosis in guinea pigs. Alternate serial paraffin sections were stained and ashed. The ashing process was carried out in a muffle furnace at a temperature of approximately 540°, about 4 hours being allowed for the incineration.

The general observation made by previous investigators that the nucleus is the part of the cell richest in ash, was confirmed. The

[2] Trendelenburg, P., Die Hormone, Julius Springer, 1929, 1, 244.

[1] Policard, A., and Doubrow, S., *Ann. d'anat. path. med.-chir.*, 1924, **1**, 163; Policard, A., *Protoplasma*, 1929, **7**, 464.

[2] Scott, G. H., *Compt. rend. soc. biol.*, 1930, **190**, 1073, 1323; PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 349; Scott, G. H., and Horning, E. S., *Am. J. Path.*, 1932, **8**, 329.