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Antagonism of the Pressor Action of Ephedrine by Cocaine.

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Certain results with excised organs and the intact circulation in this laboratory have given rise to the suspicion that ephedrine is not invariably sympathomimetic in action. That is, the responses have not always corresponded to sympathetic nerve stimulation, and have differed from those of epinephrine on the same organs or functions. On Dr. Hanzlik's suggestion, I have tested ephedrine in cocainized animals in which sensitization occurs to the pressor action of epinephrine (sympathomimetic) with a simultaneous desensitization to tyramine (musculotropic) as described recently by Tainter and Chang.[1]

The results obtained were as follows: At the end of from 10 to 15 minutes after hypodermic injection of from 6 to 30 mgm. per kilo of cocaine, the blood pressure rises from ephedrine and tyramine in a dog, a rabbit and 2 cats were not obtained, or were much less, while the rises from epinephrine were much greater than before cocaine. From 3 to 10 times the control doses (1.5 to 5 mgm. per kilo) of ephedrine gave principally a fall of blood pressure after cocaine, or in other words, a reversal of the original pressor to a depressor action. At the same time, the heart was slowed or irregular in some of the animals and there was no definite indication of a peripheral vasodilatation, as indicated by oncometric changes. Presumably, therefore, the abolition and the reversal of the pressor action were mediated through diminished functional efficiency of the heart. The striking difference from epinephrine was the complete absence of a cocaine sensitization of the pressor action of

ephedrine, indicating that ephedrine, just like tyramine, is not sympathomimetic.

These results, it is believed, further establish the value of the cocainized organism as a useful biological test object for determining the sympathomimetic action of drugs. From the standpoint of the relationship of chemical composition and structure to physiological action, and so far as the pressor action under this test is concerned, ephedrine and epinephrine are not identical pharmacologically, since the mechanisms of their actions are different; and chemically, though similar, they are also different. The reversal of the pressor action of ephedrine under cocaine indicates the need of caution in the use of ephedrine in the treatment of shock and collapse, especially when these conditions occur during cocaine anesthesia, or whenever cocaine has been absorbed.

Figures 1 and 2 illustrate typical blood pressure responses to epinephrine, tyramine and ephedrine before and after cocaine in a cat.

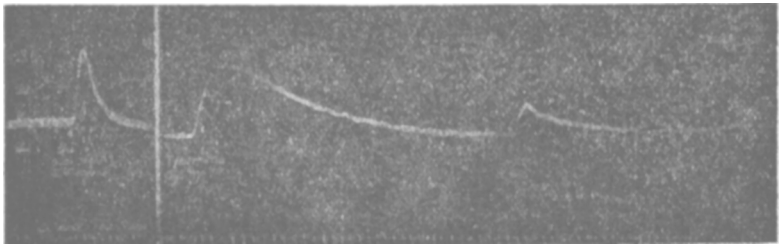

FIG. 1.

Pressor effects produced by epinephrine, tyramine and ephedrine in a urethanized cat (2.00 kg.).

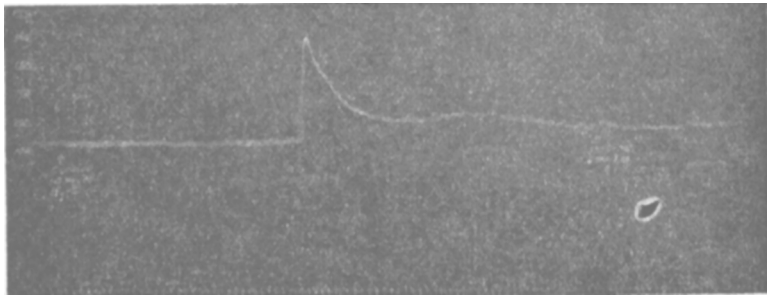

FIG. 2.

Pressor effects of ephedrine increased, and of tyramine and ephedrine abolished, by cocaine in the same cat. Records reduced to 1/3.

[1] Tainter, M. L., and Chang, D. K., *J. Pharm. Exp. Therap.*, 1927, xxx, 193.