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A striking cocaine-tyramine antagonism.

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Pharmacologically, tyramine and epinephrine appear to be similar, but not identical, in several directions. They are, of course, closely related chemically. A difference between the two drugs can be readily demonstrated in cocainized animals. Whereas ineffective doses of cocaine greatly increase (sensitize) the blood pressure response to epinephrine, they prevent (antagonize) that to tyramine in the same animal. The prevention of tyramine action by cocaine was discovered recently by us in connection with a study of tyramine action. Pending further study of its mechanism, we desire to make a preliminary report of our results at this time.

The antagonism has been demonstrated in dogs, cats and rabbits, being more marked in dogs and cats than in rabbits, whose response to tyramine is more variable. The dosage of tyramine used ranged from 0.2 to 0.5 mg. per kilo intravenously and of cocaine from 4 to 22.5 mg. per kilo subcutaneously. As a rule, the dosage of cocaine used produced little or no change in blood pressure, pulse rate, respiration and rectal temperature, and no symptoms. In about 10 minutes after the hypodermic injection of an ineffective dose of cocaine (10 mg. per kilo), the rise of blood pressure from tyramine was no longer demonstrable. The antagonism persisted from one to three hours after the administration of cocaine. This action of cocaine appeared to be rather specific, for large doses of other local anesthetics, namely procaine, butyn, and saligenin, did not prevent the tyramine rise of blood pressure in the same animals. The antagonism is not due to paralysis or depression of the sympathetics of the blood vessels, because epinephrine gave a more marked rise of blood pressure after cocaine (sensitization) than before, and stimulation of the sciatic nerve produced the usual blood pressure rise. The vessels of the perfused rabbit's ear continued to be constricted after treatment with high concentrations of cocaine. Provisionally, it appears that the antagonism is systemic, but the adrenals are not involved, since the phenomenon has been demonstrated in adrenalectomized cats. Final conclusions are reserved until the study is completed.