Translation from French

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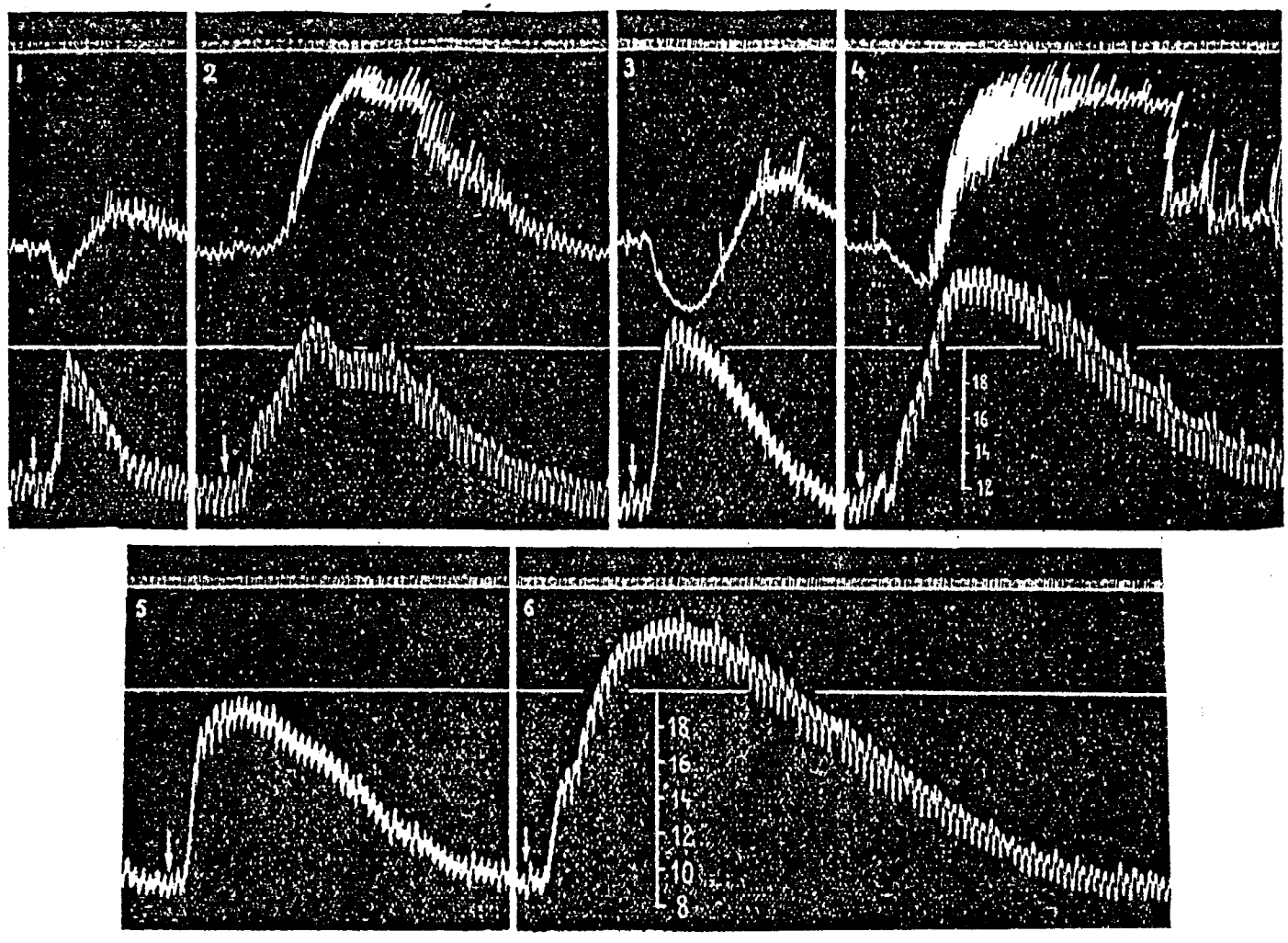
PHARMACODYNAMICS. Difference between the pharmacological action of ibogaine and that of cocaine. Communication from Mr. Raymond-Hamet, presented by Mr. Paul Portier.

Previously, we showed that, like cocaine, ibogaine suppresses more or less completely the hypertensive effects of carotid occlusion and increases the rise in pressure that follows the injection of epinephrine.

Since Tainter and Chang had observed that cocaine acts in opposite ways on hypertension produced by tyramine and hypertension produced by epinephrine, reducing the latter while it increases the former, it occurred to us that we should determine whether or not the same is true of ibogaine. Thus, we found that contrary to cocaine, the crystallized Iboga alkaloid markedly enhances the hypertensive action of tyramine at the same time that it reinfoces its renal vasoconstrictive effects. This is shown by the tracing reproduced herewith.

Initially, an injection of 0.007 mg of epinephrine had increased carotid pressure from 128 to 199 mm Hg (an increase of 71 mm Hg), while an injection of 2 mg of tyramine had raised it from 127 to 218 mm Hg (i.e., 91 mm Hg). When the animal had been given 6 mg/kg of ibogaine hydrochloride, epinephrine in the same dose as at the start of the experiment raised carotid pressure from 121 to 218 mm Hg (that is, by 97 mm Hg), while tyramine also in the same dose as previously increased it from 120 to 245 mm Hg (that is, 125 mm Hg above its baseline level. Lastly, when the animal was given a total dose of



Experiment of May 29, 1940 - Dog of 9 kg anesthetized with chloralose (12 mg/kg), operated on by bilateral vagotomy at the neck and kept on artificial respirator. Lines 1 and 4: time in seconds . Line 2: Variations in volume of kidney recorded with a Hallion and Comte oncograph modified by us. Lines 3 and 5: changes in carotid pressure recorded with a mercury manometer. At the points marked by arrows, injections were made in the saphenous vein: at 1, 3 and 5, 0.007 mg of epinephrine, and at 2, 4 and 6, 2 mg of tyramine. The animal received the following intravenous injections: between tracings 2 and 3, first 18 and then 36 mg, and between tracings 4 and 5, 72 and then 54 mg of ibogaine hydrochloride. Tracings reduced by 50%.

20 mg/kg of ibogaine hydrochloride, the carotid pressure went up from 98 to 198 mm Hg after injection of still the same dose of epinephrine, and from 99 to 246 mm Hg after injection of the same dose of tyramine as previously, so that the hypertension was 100 mm Hg with the former and 147 mm Hg with the latter. The increase in the hypertensive effects which, after injection of 6 mg/kg of ibogaine hydrochloride, was 36.76% with epinephrine and 37.36% with tyramine, became 40.84% with epinephrine and 61.53% with tyramine when the animal had received a total of 20 mg per kg of this salt. Thus, in this experiment, ibogaine increased tyramine-induced hypertension to a greater degree than the hypertension produced by epinephrine.

We should add that in this experiment ibogaine increased not only the maximum elevation but also the duration of hypertension induced both by tyramine and epinephrine. Finally, we should mention that in this same animal, the crystallized alkaloid of Iboga reinforced not only renal vasoconstriction produced by epinephrine but also the one produced by tyramine. With epinephrine, this reinforcement was evidenced both by a deepening and a broadening of the depression of the oncographic tracing which corresponds to a reduction in the volume of the kidney. With tyramine, the vasoconstriction, which marks the initial stage of the renal action of tyramine, was only manifested by an extremely slight weakening of renal pulse and by the coexistence of an insignificant increase in the volume of this organ and a very strong rise in carotid pressure prior to treatment with ibogaine; after treatment with ibogaine, it was manifested by a very marked decrease in the volume of this organ.

Thus, ibogaine increases the hypertensive action of both tyramine and epinephrine and in this regard demonstrates a physiological action

that differs from that of cocaine and appears closer to that of sparteine which, according to Hazard, can increase but may also sometimes have no effect upon, or may even reduce, hypertension induced by tyramine.