

only to the strong rise which sets in, as is known, immediately after injection of that substance. With the onset of the descent of pressure the depressor action of the depressor nerve becomes more and more effective. Here the inefficiency of the stimulation of the depressor may be due merely to the inability of the depressor nerve to overcome the high pressure. It is different, however, with the action of the hypophysis. Here the rise of blood pressure develops as a rule, gradually and sometimes it is even preceded by a fall. Furthermore in some instances the rise is comparatively insignificant. Nevertheless in all these conditions there is definite evidence of a striking reduction of the irritability of the depressor. We are therefore, for the present, inclined to look upon the discovered reduction of the irritability of the depressor nerve as a confirmation of our hypothesis that the infundibular portion of the hypophysis reduces the irritability of vasodilators. We may mention that studies upon the vasomotor effects of stimulations of the central end of the vagus nerve in dogs, which we shall not discuss here in detail, seem to furnish a further confirmation of this view. As to the locality where the hypophysis develops its action, whether upon the central or peripheral mechanisms or upon both, we shall not discuss at present.

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On the reduction of toxicity of strychnin by the simultaneous administration of large quantities of fluid.

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In the course of some experiments on adrenalin glycosuria in which the simultaneous injection of blood, serum or lymph with adrenalin was studied, it became manifest that the significance of the factor of dilution had to be previously established. It was thought that the study of the effect of dilution upon strychnin poisoning would throw some light upon this. The definite and instructive results which were obtained will be stated here very briefly.

Controls.—Six rabbits received subcutaneously 0.45 mg. strychnin per kilogram body weight. All six had convulsions, with fatal termination in three. Nine animals received 0.5 mg. per kilo; all had convulsions, terminating fatally in four. In 15 controls, then, a dose of 0.5 mg. strychnin or less per kilo body weight brought on convulsions in every one and a fatal termination in 7; in other words 0.5 mg. strychnin proved to be toxic in 100 per cent. and fatal in 47 per cent.

Strychnin diluted in 100 c.c. of normal saline.—Ten rabbits received subcutaneously doses of strychnin varying between 0.7 and 0.84 mg. per kilo body weight diluted in 100 c.c. of 0.9 per cent. sodium chlorid. Of these only two had convulsions, one of which died. In other words, strychnin in great dilution is considerably less toxic; doses which exceed the minimal fatal dose proved to be toxic only in 20 per cent. and fatal in 10 per cent.

Strychnin and saline injected in separate places.—In a series of eleven rabbits each received subcutaneously 0.5 mg. strychnin per kilo body weight at one point shortly after having been injected with 100 c.c. of 0.9 per cent. sodium chlorid at another place. Of these only three had convulsions and only one died. In other words, when 100 c.c. of saline was injected in another part of the body, a dose of 0.5 mg. per kilo of body weight, which in controls proved toxic in 100 per cent. and fatal in 47 per cent., was toxic only in 27 per cent. and fatal in 9 per cent.

Strychnin subcutaneously and water given by mouth.—Eight rabbits received 0.5 mg. strychnin per kilo body weight subcutaneously shortly after 100 to 150 c.c. of water had been given by mouth. Of these animals only two had convulsions and none died, that is, in these cases 0.5 mg. strychnin proved to be toxic only in 25 per cent. and caused no fatalities. Twelve animals were given strychnin subcutaneously, in doses varying between 0.52 and 0.56 mg. per kilo body weight, receiving at the same time 100 c.c. of water by mouth. Of these animals four had convulsions and none died. In other words even doses which definitely exceed the sure toxic dose of 0.5 mg. per kilo, proved toxic only in 33 per cent. with no fatalities at all, when at the same time, a comparatively large quantity of water was given by mouth.

These experiments seem to demonstrate conclusively that the

toxicity of strychnin is definitely reduced not only when it is administered in great dilution, but also when saline or water is administered nearly simultaneously in other parts of the body, thus, perhaps, diluting the poison within the circulation. These results are of general theoretical interest and have obviously also a practical bearing, neither of which we shall discuss here.

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The influence of the infundibular portion of the hypophysis upon the pupil.

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The action of the extract of the hypophysis is similar to that of adrenal extract in the first place by the influence which both exert upon blood pressure. There seems to be also some similarity in their action upon the uterus and intestines. With regard to the action of hypophysis upon the frog's pupil which, as is well known, becomes definitely dilated by adrenalin, opinions differ. While Cramer and others report a dilatation, Kepinow and Gottlieb recently stated that in their hands the extract of the hypophysis caused a constriction of the frog's pupil. In my own observations upon the enucleated bulbi from *Rana pipiens*, heated and unheated *pituitrin* (Parke Davis & Co., prepared from the infundibular portion of the hypophysis) *in most instances caused a dilatation of the pupil*. The extent of the dilatation varied greatly in various eyes and was never as striking as is observed under the influence of adrenalin. In a smaller number no dilatation of the pupils took place; *but in no instance have I observed a miosis following the bathing of the bulbi in pituitrin*.

A very striking test is the action of adrenalin on the pupil of mammals (rabbit or cats) on the side on which the superior cervical ganglion had been removed 24 hours or longer. If a sufficient dose was used, that pupil showed a maximal dilatation which may last for hours, while the pupil on the normal side remains unchanged. I have studied this test with *pituitrin*. In six rabbits