foetal life. Sixteen, 17, and 18-day embryos were similarly injected. Gonads of both sexes were preserved for sectioning at various stages of both injected and non-injected animals. All material was fixed in Bouin's solution.

Prenatal injection in no way hastened the differentiation in the gonad. It is thus evident that the gonad of the rat foetus is incapable of response to the pituitary hormone. No evidence of sexual maturity was observed in either sex until the tenth day of postnatal life, when the effect was most pronounced in the male. This effect evinced itself in an apparent increase in tubule length as well as by a considerable thickening of the tubular wall. There is an undoubted increase in the size of the interstitial cells, and the tissue presents a dense and closely-packed appearance. We attribute this close-packed appearance to the increase in length and diameter of the tubules. No reconstructions have as yet been made to render this point a certainty.

In the ovary the earliest advance in maturity of the injected animals over the controls appeared at approximately the fifteenth day. No corpora lutea were present but the follicles are larger in diameter and more nearly approaching maturity than in the normal animal if judged by the amount of follicular fluid present. At the twentieth day this precocious development is more marked. In no case were corpora lutea observed nor could eggs be discerned within the lumen of the sectioned tube.

On the basis of the above results, the physiological effect of the pituitary hormone upon the gonad first shows itself in *both* sexes between the tenth and fifteenth days of postnatal life.

[1] Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1927, xl, 159.

[2] Nicholas, J. S., *Anat. Rec.*, 1925, xxxi, 385.

3922

Studies on Quinine and Quinidine V. Do They Have a Specific Action on Autonomic Nerve Ends?

ERWIN E. NELSON.

From the Department of Materia Medica and Therapeutics, University of Michigan Medical School.

In an earlier paper in this series[1] it was shown that epinephrine loses part or all of its pressor activity in dogs following injections of quinine or quinidine because of a partial or complete paralysis of

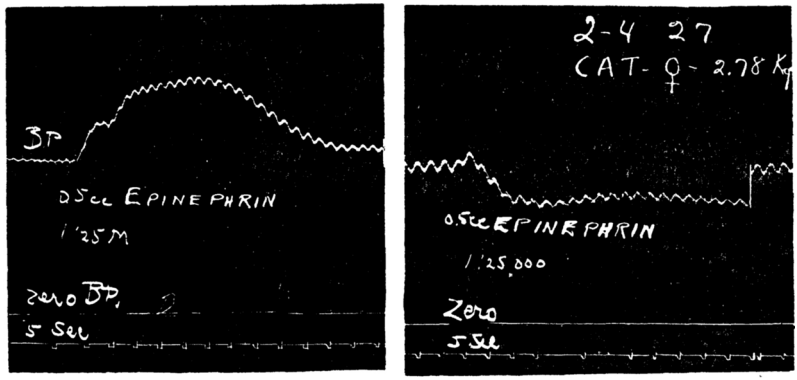

FIG. 1.

Vasomotor reversal in the cat. Between the two injections of epinephrine, 12 mg. Quinidine hydrochloride were injected. Morphine-urethane anesthesia.

the peripheral vasomotor mechanism. This was localized as being on the endings because pituitary solution was still effective in raising the blood pressure. The work has been extended to cats, and it has been found that there is not only a loss of pressor activity but also in some cases a very clear cut vasomotor reversal. Figure 1 illustrates such a case. Here approximately 3 mg. of quinidine per kilo have completely reversed the action of epinephrine. In other similar experiments this same result has been obtained not only from the injection of epinephrine, but also from stimulation of the splanchnics. These findings in cats and dogs suggest a similarity in action between quinine (or quinidine) and the ergot alkaloids. When the reaction of the rabbit uterus to epinephrine before and after quinine or quinidine was examined, there was again noted this reversal. This phenomenon has also been noted by Stake[2] and Langecker.[3] The isolated uterus of the virgin cat which relaxes to epinephrine, gave a greater degree of relaxation after administration of quinine. In 2 experiments the stimulant action of epinephrine for the retractor penis of the dog has been reversed. Because of these positive findings the experiments have been further extended to determine whether quinine and quinidine could be said to act specifically on the motor divisions of the sympathetics. The experiments have been uniformly negative. It has not been possible to show any antagonism for the action of epinephrine or the cervical sympathetic on the dilator iridis or the orbital smooth muscle (cats, rabbits). Neither the sympathetic secretion (cats, dogs) nor the chorda secretion (dogs) from the submaxillary gland is altered in amount by quinine. The augmentor effect of epinephrine on the heart persists after these alkaloids. And finally epinephrine pro-

duces its characteristic rise in blood sugar after quinine though this has been shown to be prevented easily by ergotoxin or ergotamine. When quinine bisulphate, 20 mg. per kilogram is given intravenously to fasting rabbits, there is a rise in blood sugar, the maximum value rarely being as high as 200 mg. per 100 cc. This maximum is reached in from 60 to 90 minutes, after which it gradually falls. Epinephrine, 0.2 cc. of 1:10,000, injected through a period of 10 minutes, intravenously, at the time of maximum quinine effect, produces a second increase, which may go above 300 mg. If quinine has any antagonism for this effect of epinephrine, it is very slight.

Because of these negative findings, no further antagonisms have been studied, for though others may be found there are sufficient exceptions to make impossible the generalization suggested earlier.[4] Quinine and quinidine, though apparently having a selective action on the motor sympathetics to the blood vessels in cats and dogs, do not have such an action for all the motor fibers of the sympathetic division.

[1] Nelson, E. E., *Arch. intern. de Pharmacodyn. et de Therap.*, 1927, xxxiii, 197.

[2] Stake, T., *Compt. Rend. Soc. Biol.*, 1926, xciv, 954.

[3] Langecker, H., *Arch. exp. Path. u. Pharmakol.*, 1926, cxviii, 49.

[4] Nelson, E. E., *J. Pharm. Exp. Therap.*, 1927, xxxi, 209.