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Ephedrine-Epinephrine Antagonism.

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Antagonism of epinephrine action by high concentrations of ephedrine (1:9000-1:6000) has been described by several European workers,¹ using Magnus preparations of excised small intestine of rabbit and cat and of excised guinea pig uterus. In extending the study of the ephedrine-epinephrine antagonism to Magnus strip preparations of small intestine, colon and uterus of various species (cat, rabbit, dog, rat, guinea pig) I have found that it occurs with all these organs. Furthermore, not only did high concentrations of ephedrine antagonize epinephrine inhibition, but low concentrations as well (1:100,000-1:25,000), and often to a marked degree. Segments of uterus of the rabbit and of the pregnant cat, treated with ergot alkaloids, to produce an inhibitory response to epinephrine, exhibited the antagonism as completely as did the organs whose normal response to epinephrine is one of inhibition or relaxation. The "depressant" action of epinephrine (1:50,000,000-1:1,000,000) on all these organs was opposed by ephedrine, whether applied to the tissues before, or a few seconds after, the application of epinephrine.

"Depression" of segments of rabbit duodenum by a mixture of epinephrine and ephedrine occurred, although the same concentrations applied separately and in sequence, exhibited the usual antagonism. This indicates that there is no chemical action between the

¹ Nagel, A., *Arch. exp. Path. Pharm.*, 1925, cx, 128. Kreitmair, H., *Arch. exp. Path. Pharm.*, 1927, cxx, 189. Reinitz, N., *Compt. rend. soc. biol.*, 1928, xcvi, 809.

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2 drugs outside the tissues. Antagonism of epinephrine "depression" by ephedrine occurred whether ephedrine itself caused contraction, relaxation or no demonstrable effect on the activity of the muscle. This fact, and the fact that low concentrations as well as high concentrations of ephedrine were effective in antagonizing epinephrine do not support the opinion of Nagel¹ that the antagonism is due to a muscle stimulating action of ephedrine. It would seem rather that it is due to some as yet ill-defined action of ephedrine on the sympathetic nerve-muscle connections.