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Action of Ephedrine and Pseudoephedrine Upon the Bronchial Muscle.

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Using our modified method of the isolated lung perfusion described by Sollmann and Von Oettingen,¹ we studied the peripheral action of ephedrine and pseudoephedrine on rabbit bronchial muscle. The arrangement of the perfusion was similar to that of Sollmann and Von Oettingen, but the borders of the lung were trimmed with sharp scissors so that the perfusion fluid was allowed to drain freely. The lung was lightly supported with a funnel covered with moist cotton to prevent drying, drops per minute through the funnel being reckoned as the rate of the bronchial outflow. The drugs took from half to one minute to reach the outflow, and 4 to 5 minutes for the concentration of drug of the outflow to be the same as that of the inflow. After 1 to 2 hours of perfusion with Tyrode solution, when the rate of outflow was 50 to 80 drops per minute, and when it had remained nearly constant for over 10 minutes, the perfusion of the ephedrine-Tyrode solution was started, and allowed to continue for 20 to 30 minutes (pH of ephedrine and Tyrode solution was found to be the same). Bronchial constriction was indicated by a decrease of outflow, and dilation by an increase. The bronchial muscle under this condition was found to be exceedingly sensitive to drugs, comparing with the method of Sollmann and Von Oettingen. After 6 to 7 hours of perfusion the bronchioles still responded to drugs. Injection of 0.5 cc. of pilocarpine 1:1,000,000 or atropine 1:1,000,000 into the connecting tube between lung and perfusion apparatus caused respectively a distinct constriction and dilation of the bronchioles.

The response of the bronchial muscle to ephedrine varied with the dosage. Perfusion with highly diluted concentrations, such as 1:1,000,000 to 1:5,000,000 in 6 experiments produced a definite bronchial dilatation, and the effect of 1:1,000,000 was more distinct than that of the more dilute solution. Comparing this effect with the action of ephedrine on the circulation and other smooth muscles the bronchial dilation is probably a sympathetic action. Perfusion

¹ Sollmann, T., and Von Oettingen, W. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1928, xxv, 692.

with moderate concentrations of ephedrine, namely 1:10,000 to 1:200,000, in 7 experiments uniformly caused bronchial constriction, and the effect of 1:10,000 was stronger than that of 1:100,000. In 4 experiments, atropine 1:500,000, perfused for 6 to 10 minutes previous to ephedrine, had no influence on the bronchial constricting effect of ephedrine. In this instance the broncho-constricting effect of ephedrine is probably a muscular effect and its sympathetic action is apparently not present. Perfusion with high concentrations, *i. e.*, 1:200 to 1:2,000, in 9 experiments caused either marked constriction (4 cases), or marked dilatation of the bronchioles, depending on the condition of the bronchial muscle and its sensitivity to drugs. The constricting effect was more pronounced than that from moderate concentrations of ephedrine. The marked dilatation may be due to direct muscular depression, as the subsequent injection of barium chloride produced no effect.

The effect of pseudoephedrine on the bronchial muscle is similar to that of ephedrine. Concentrations between 1:1,000,000 and 1:100,000, in 5 experiments produced bronchial dilatation in sensitive bronchial preparations, but no effect in insensitive ones. The perfusion with 1:10,000 and with 1:2,000 each in 2 experiments produced a regular distinct bronchial constriction, and the constricting effect of 1:10,000 was apparently stronger than the same concentration of ephedrine. Pseudoephedrine seems to be more muscletropic than ephedrine.

We conclude that ephedrine is a sympathomimetic and muscletropic drug, and this fact confirms further the observation of Pak and Read² on the blood pressor action. Tainter³ and others claimed ephedrine to be a pure muscletropic drug, while on the other hand, Chen⁴ and others believed it to be a sympathomimetic amine. These divergent conclusions are possibly due to dissimilar dosage, one may have used large doses in which the sympathetic action was overpowered by strong muscular action, or, on the other hand, small dosage may have been used, which produces a pure sympathetic effect.

² Pak, C., and Read, B. E., *Chinese J. Physiol.*, 1928, ii, 1; 1929, iii, 435.

³ Tainter, M. L., *J. Pharm. Exp. Therap.*, 1929, xxxvi, 569.

⁴ Chen, K. K., *J. Pharm. Exp. Therap.*, 1928, xxxiii, 219.