References

POWIS, G. (1973). Binding of catecholamines to connective tissue and the effect upon the responses of blood vessels to noradrenaline and to nerve stimulation. *J. Physiol., Lond.*, **234**, 145-162.

SULKOWSKI, S.R. & HASERICK, J.R. (1964). Simulated systemic lupus erythematosus from degraded tetracycline. *J. Am. med. Ass.*, **189**, 152-154.

Adrenergic blockade and the pulmonary pressor response to lactic acid

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Vasoconstriction in the lung is an important protective response. Its mechanism in relation to drugs and hypoxia has been studied by others.

We find that the pulmonary vascular bed in the sheep responds to small doses of 4 ml 0.75 molar lactic acid with a 50% or greater increase in mean pulmonary artery pressure ($P\bar{p}a$). The lactic acid is injected into the jugular vein (J.V.) and the response follows in nine seconds. The $P\bar{p}a$ returns to near the previous level in four minutes. The test can be repeated many times provided sodium bicarbonate is given to maintain blood pH at or above 7.3. The sheep are anaesthetized with halothane and ventilated. Pressures are recorded continuously from the pulmonary artery and left ventricle.

Previous experiments have shown that the rise in Ppa is not due to an increase in flow or elevation of left atrial pressure but the change in Ppa reflects a change in pulmonary vascular resistance. It is of interest that lactic acid is a vasoconstrictor in the pulmonary vascular bed and a vasodilator in the skeletal muscular bed.

The injection of 10 mg phentolamine into the J.V. results 5 to 10 min later in marked reduction or abolition of the response to lactic acid.

Infusion of phenoxybenzamine, 30 mg in 200 ml of saline in 30 min, results 75 min later in the disappearance of the pressor response to lactic acid.

Reserpine 2.5 mg prevented the response after a variable time of the order of two hours. Atropine (12-17 mg) had no effect on the response.

Thus α-adrenoceptor blockade prevents the expected increase in $P\bar{p}a$ on injection of lactic acid and the effect of reserpine suggests that catecholamines play a part in the response.

Isoprenaline infusion (2 to 4 μg doses in 1 to 2 min), sufficient to raise the heart rate 40 beats per min, immediately abolishes the $P\bar{p}a$ response to lactic acid. We find, like others, that β-adrenoceptor blockade restores some of the pressor response removed by α-adrenoceptor blockade.

Several workers (Barer & McCurnie, 1969; Hyman, Woolverton, Guth & Ichinose, 1971) have demonstrated a pulmonary pressor response to various acids and the common factor is the hydrogen ion. Alpha adrenoceptors are particularly concerned in the response but the part played by β-adrenoceptors has yet to be determined. The consistent delay of 9 to 11 s in the appearance of the response remains unexplained.

References

BARRER, G.R. & McCURRIE, J.R. (1969). Pulmonary vasomotor responses in the cat: The effects and interrelationships of drugs, hypoxia and hypercopnia. *Q. Jl. exp. Physiol.*, **54**, 156-172.

HYMAN, A.L., WOOLVERTON, W.D., GUTH, P.S. & ICHINOSE, H. (1971). The pulmonary vasopressor response to decreases in blood pH in intact dogs. *J. clin. Invest.*, **50**, 1028-1043.