References

Bertler, Å., Carlsson, A. & Rosengren, E. (1958). *Acta physiol. scand.*, **44**, 273–292.
Bertler, Å. & Rosengren, E. (1959). *Experientia*, **15**, 182.
Carlsson, A. & Corrodi, H. (1964). *Helv. chim. acta*, **47**, 1340–1349.
Carlsson, A., Corrodi, H. & Waldeck, B. (1963). *Ibid.*, **46**, 2271–2285.
Carlsson, A. & Lindqvist, M. (1962). *Acta physiol. scand.*, **54**, 87–94.
Corrodi, H. & Hanson, L. (1966). *Ibid.* In the press.
Falck, B. (1962). *Ibid.*, **56**, Suppl. 197, 1–25.
Falck, B., Hillarp, N. Å., Thieme, G. & Torp, A. (1962). *J. Histochem. Cytochem.*, **10**, 348–354.
Hillarp, N. Å., Fuxe, K. & Dahlström, A. (1965). Paper presented at the *International Symposium on mechanisms of release of biogenic amines.* Stockholm, February 21–24.
Roos, B. E. & Werdinius, B. (1963). *Life Sci.*, **2**, 92–96.

2-Deoxyglucose and inflammation

SIR,—2-Deoxyglucose reduces oedema formation produced by injecting dextran into rats (Goth, 1959), and also inhibits the development of erythema in guinea-pigs exposed to ultraviolet irradiation (Görög & Szporny, 1964). The anti-inflammatory activity of 2-deoxyglucose is generally supposed to be connected with its effects on carbohydrate metabolism. However, 2-deoxyglucose also stimulates the release of catecholamines from the adrenal medulla (Brown & Bachrach, 1959; Hokfelt & Bydgeman, 1961), and evidence is presented which suggests that the anti-oedematous effect of this compound is mediated through this latter mechanism.

Groups of six female rats, 140–170 g, received an intraperitoneal injection of saline or 2-deoxyglucose, 250 mg/kg, 30 min before an injection beneath the left hind paw of 0·1 ml of the supernatant fluid from a 5% suspension of Brewers yeast. Foot volumes were recorded plethysmometrically before and 3/4 hr after the injection. Adrenalectomy or adrenal demedullation was performed 1 week before the experiment, and the adrenalectomised rats were maintained on 1% saline instead of tap water. Blood was taken by cardiac puncture at the time of the second foot-volume measurement. The % inhibition of oedema and % increase in blood sugar caused by 2-deoxyglucose were, in normal 58·9 and 81·7, in adrenalectomised 6·2 and 12·2 and in adrenal-demedullated rats 1·1 and 15·7 respectively. In adrenalectomised and demedullated animals this compound has no anti-oedematous effect and its hyperglycaemic activity is reduced but not abolished. Other irritants such as formaldehyde or silver nitrate have been used and the results were similar.

Propranolol, 10 mg/kg i.m., given 1 hr before 0·1 ml of the yeast extract, antagonises the anti-oedematous activity of adrenaline, 0·5 mg/kg s.c., and 2-deoxyglucose, 250 mg/kg i.p., given 30 min before the yeast extract. Propranolol, by itself does not affect oedema formation, a % inhibition of 3·1 being obtained, nor does it modify the anti-oedematous effects of cyproheptadine, phenylbutazone or hydrocortisone (Kellett, 1966). 2-Deoxyglucose caused a 62·9% inhibition of oedema, adrenaline 66·3, deoxyglucose + propranolol 27·4 and adrenaline + propranolol 29·3% inhibition. There were six rats per group.

While the assumption that 2-deoxyglucose inhibits inflammatory reactions by an effect on carbohydrate metabolism may still be correct, it seems that a direct effect on glycolysis is unlikely to be important. It is possible, however, that an indirect effect on carbohydrate metabolism, through catecholamine release from the adrenal medulla, may be involved. Impaired disposition of a glucose load is seen after the injection of 2-deoxyglucose into normal rats, but

this effect is absent in adrenal demedullated animals (Brown & Bachrach, 1959). If, as Goth (1959) suggests, the anti-oedematous effect of 2-deoxyglucose depends on changes in the permeability of cell membranes to glucose and related macromolecules, then adrenaline may be involved in maintaining the decreased permeability to these substances which exists when 2-deoxyglucose is given to normal animals.

2-Deoxyglucose was less active in the ultraviolet erythema test than in the rat-paw test. Intraperitoneal doses of 400 mg/kg of 2-deoxyglucose were needed for consistent suppression of the erythema. Adrenaline, 1 mg/kg s.c., also inhibited the development of erythema following ultraviolet irradiation, but we have so far failed to antagonise the adrenaline or 2-deoxyglucose responses using large doses of pronethalol, propranolol or dihydroergotamine.

It is impossible to draw any conclusion from these experiments about the mode of action of 2-deoxyglucose in the ultraviolet erythema test, but it would be unwise to assume that its effect is due solely to alterations in carbohydrate metabolism (Görög & Szporny, 1964), since an effect on the adrenal medulla may also be involved.

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References

Brown, J. & Bachrach, H. L. (1959). *Proc. Soc. exp. Biol. Med.*, **100**, 641–643.
Görög, P. & Szporny, Z. (1964). *J. Pharm. Pharmac.*, **16**, 635–636.
Goth, A. (1959). *Am. J. Physiol.*, **197**, 1056–1058.
Hokfelt, B. & Bydgeman, S. (1961). *Proc. Soc. exp. Biol. Med.*, **106**, 537–539.
Kellett, D. N. (1966). *Br. J. Pharmac. Chemother.*, in the press.