Effects of Prostaglandin E_2 on the Uptake of ^{3}H-Thymidine in Pregnant Mice

Despite the widespread clinical use of certain prostaglandins for the termination of pregnancy and the induction of labor, little attention has been directed to the effects of these substances on fetal and maternal metabolism. Prostaglandin E_2 (PGE_2) administered to pregnant rats[1] and mice[2] induced a high incidence of fetal death and resorptions. The mechanism for this lethal action is uncertain. We report here the effects of PGE_2 on the uptake of ^{3}H-thymidine in maternal and fetal tissues of mice.

Materials and methods. Prostaglandin E_2 (50 or 100 µg) was administered s.c. to pregnant Swiss Webster mice from day 8 through 12 of gestation. Another group of mice received the solvent alone and served as controls. The animals were killed on the last day of treatment 1 h after an i.v. administration of 1 µCi/g ^{3}H-thymidine (New England Nuclear; Specific Activity: 6.7 C/m*M*). Selected maternal tissues and the conceptuses were excised under a dissecting microscope and processed subsequently to determine the concentration of radioactivity. The tissue samples were pooled and weighed immediately after removal, dissolved in NCS and neutralized with acetic acid. 10 ml of a scintillation cocktail (5 g PPO; 0.5 g POPOP; 250 ml ethylene glycol monomethyl ether; 750 ml toluene) was added and the samples were counted three times for 10 min in a Beckman LS 150 Liquid Scintillation Counter.

Uptake of ^{3}H-thymidine in pregnant mice treated with prostaglandin E_2

Tissues	Control	Prostaglandin-treated	
		50 µg	100 µg
Maternal			
Brain	303.2 ± 50.4	210.0 ± 11.5	152.5 ± 10.1
P[b]		< 0.05	< 0.01
Lung	387.6 ± 68.8	252.4 ± 54.6	211.3 ± 31.1
P		< 0.05	< 0.05
Liver	653.7 ± 122.5	591.1 ± 101.4	520.2 ± 98.3
P		NS	< 0.05
Kidney	451.5 ± 75.3	303.4 ± 82.7	401.4 ± 90.5
P		< 0.05	NS
Spleen	1881.2 ± 183.4[a]	1555.8 ± 190.3	922.0 ± 167.9
P		< 0.05	< 0.01
Embryos	662.9 ± 81.1	324.6 ± 53.5	
P		< 0.01	

[a] Mean counts per min (cpm) per mg wet tissue weight. Standard error of the mean on the basis of 10 min counts; [b] *P*, significance of difference from the control; NS, not significant.

Results and discussion. A summary of our findings is presented in the Table. The uptake of ^{3}H-thymidine in maternal and embryonic tissues was significantly reduced following pre-treatment with the prostaglandin.

Inhibition of ^{3}H-thymidine uptake in maternal liver, brain and spleen showed a dose dependent relationship. The uptake of ^{3}H-thymidine was markedly reduced in the embryos. However, a correlation between the uptake of ^{3}H-thymidine in the 2 treatment groups was not possible, since all fetuses had been resorbed at the higher dose level.

These preliminary findings suggest that PGE_2 is capable of inhibiting DNA synthesis, either directly or indirectly. This inhibition could account for some of PGE_2 effects on the fetus and placenta during pregnancy[3,4]. Further studies of ^{3}H-thymidine, ^{3}H-uridine, and ^{3}H-leucine at different gestational periods are in progress.

Zusammenfassung. Die Behandlung von trächtigen Mäusen mit Prostaglandin E_2 führt zu einer Verminderung des Einbaus von ^{3}H-Thymidin im mütterlichen und fötalen Gewebe.

J. Clancy, jr. and T. V. N. Persaud[5]

Teratology Research Laboratory, Department of Anatomy, University of Manitoba, Winnipeg (Manitoba R3E OW3, Canada), 27 December 1973.

[1] T. V. N. Persaud, Prostaglandins *3*, 299 (1973).
[2] T. V. N. Persaud, unpublished data.
[3] J. G. Wilson, Am. J. Anat. *136*, 129 (1972).
[4] E. J. Ritter, W. J. Scott and J. G. Wilson, Teratology *7*, 219 (1973).
[5] This work was supported by the Medical Research Council of Canada. Prostaglandin E_2 was kindly donated by Dr. J. Pike, Upjohn Company, Kalamazoo, Michigan. We thank Dr. F. Bertalanffy for valuable advice.

The Response of the Adrenal Gland to Hypoglycaemia in the Conscious Calf

A technique has recently been devised which permits collection of the whole of the effluent blood from the innervated right adrenal gland in the conscious unrestrained calf[1,2]. The present paper describes experiments in which this technique has been employed to investigate the changes in glucocorticoid and catecholamine output from the gland during insulin hypoglycaemia.

Materials and methods. Insulin was injected i.v. at doses of 0.1, 0.5 or 4.0 units/kg 14–24 h after surgery. Adrenal blood flow was estimated gravimetrically and the outputs of steroids and catecholamines were then calculated from the adrenal venous plasma concentrations. Adrenaline and noradrenaline were estimated by a modification of von Euler and Lishajko's fluorimetric technique[3], glucocorticoids by competitive protein binding assay[4] and glucose enzymatically.

Results and discussion. Results of a typical experiment illustrating the characteristic responses to insulin hypoglycaemia at each dose are compared in the Figure.

[1] A. V. Edwards, R. N. Hardy and K. W. Malinowska, J. Physiol. Lond. *239*, 477 (1974).
[2] A. V. Edwards, R. N. Hardy and K. W. Malinowska, J. Physiol. Lond., in press (1974).
[3] U. S. von Euler and F. Lishajko, Acta physiol. scand. *45*, 122 (1959).
[4] K. W. Malinowska, R. N. Hardy and P. W. Nathanielsz, J. Endocr. *55*, 397 (1972).