

DISTRIBUTION OF 9-H³-PROSTAGLANDIN F_{2α} IN PREGNANT AND NON-PREGNANT SUBJECTS

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Summary

Study of three pregnant and two non-pregnant women showed no differences in distribution or elimination of injected 9-H³-prostaglandin F_{2α}. There was no selective uptake by the uterus. Measurement of radioactivity in fetal tissue samples indicated that the transfer of PGF_{2α} or its radioactive metabolites occurred freely.

A STUDY was undertaken to investigate the distribution of 9-H³-prostaglandin F_{2α} injected intravenously into women and to observe whether any difference in its distribution could be detected between pregnant and non-pregnant subjects.

PATIENTS AND METHODS

Five healthy patients, three of whom were 16-20 weeks pregnant and two not pregnant, gave informed consent to an intravenous injection of 100 μCi 9-H³-PGF_{2α} (7.5 Ci per mM) prior to an operation for pregnancy termination or/and sterilization (Table I).

After induction of anaesthesia, the labelled prostaglandin in 2 ml. of saline was injected into an antecubital vein, except in Case 1 where the injection was into a jugular vein. At approximately 1, 3, 6, 9, 12, 30 and 90 minutes after the injection 5 ml. samples of blood were withdrawn through a self-retaining intravenous needle in the opposite arm. Each blood sample was placed in a plain non-heparinized collecting bottle and the time of withdrawal was recorded.

The abdomen was opened after the first venous blood sample had been taken. Samples of skin, subcutaneous fat, rectus muscle,

myometrium, ovary and on some occasions, Fallopian tube also, were obtained. Each tissue sample was placed in a separate standard sealed container, and the time of its removal was recorded. Before hysterotomy a sample of liquor amnii was withdrawn into a syringe. After evacuation of the uterus specimens of placenta, umbilicus, cord blood and fetal skin, liver and lung were taken. In Case 3, where a twin pregnancy was terminated, samples taken from both fetuses were combined for the estimation.

About 0.5 g. wet weight of each tissue was weighed accurately and placed in a separate sealed container. The clotted blood samples were centrifuged and the serum removed. Later 0.25 ml. aliquots were taken from each sample for analysis.

Urine was collected over a twenty-four hour period after injection, in four six-hour collections. The total urine passed during each six-hour period was measured and a 0.25 ml. sample taken for analysis. Faeces from the first two bowel movements following surgery were collected, weighed and a 0.5 g. sample from each was sent for analysis.

All weighed specimens were treated in a

Model 300 Tri-carb automatic sample oxidizer and then the radioactivity was measured using a Packard 3380 scintillation counter with a Model 544 analyzer.

RESULTS

Fate of Injected 9-H³-PGF_{2x}

The serum levels of tritium during the ninety-minute period after injection are shown in Figure 1. An initial high level was followed by a rapid disappearance of radioactivity. Within 30 minutes of injection more than 95 per cent of the radioactivity had disappeared from the circulation. The fall was slightly more rapid in the pregnant subjects.

Distribution of 9-H³-PGF_{2x}

Maternal tissues. All maternal tissues were removed within 30 minutes of injection. The levels of radioactivity are shown in Table I. No relationship could be found between the

level of radioactivity in tissues and the time of their removal. Very variable quantities of radioactivity were found in both subcutaneous fat and rectus muscle, and there was no evidence of particular concentration in any other tissue.

Fetal tissues. In Table II the levels of radioactivity in fetal tissues are shown. A consistently high level of radioactivity is found in the fetal liver, but in all other tissues the levels were similar to those found in maternal tissues. In Case 5, where the fetus was removed earlier than in Cases 3 and 4, the level of radioactivity in all tissues was lowest.

Excretion

The total radioactivity measured in urine and faeces of each patient is shown in Table III. In 4 of the 5 patients, nearly all the radioactivity appeared in the urine within 24 hours, but in the fifth case only 50 per cent of the radioactivity was detected in the urine during this time. Less

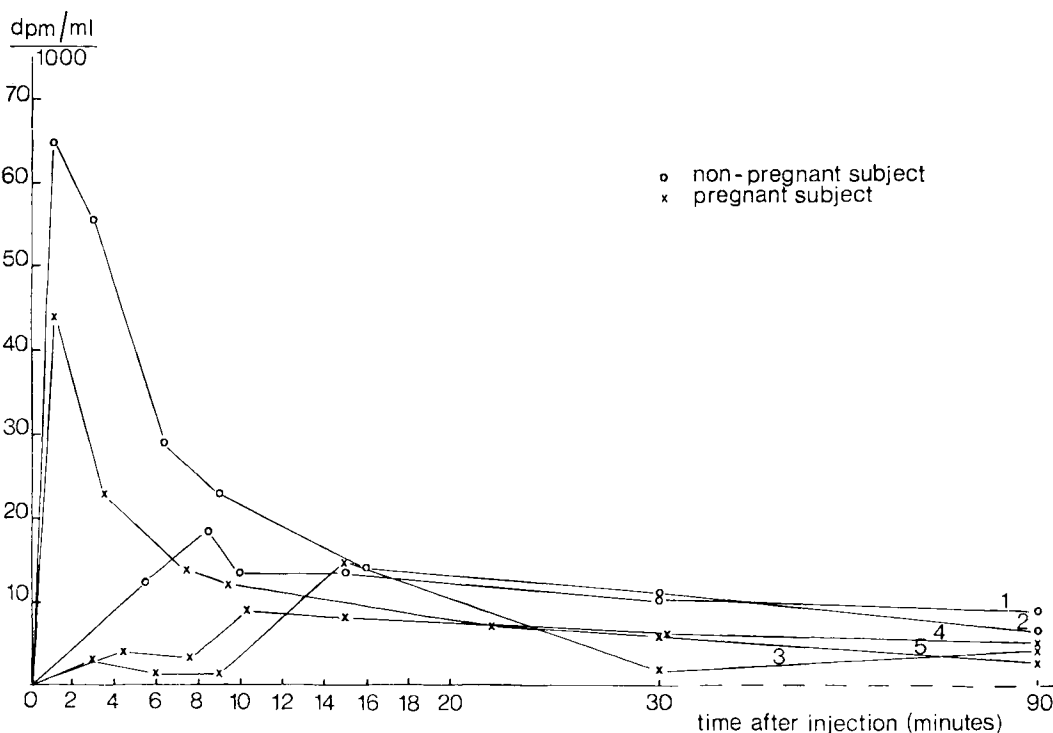


FIG. 1

Blood levels of H³ following intravenous injection of 9-H³-PGF_{2x}. (Numbers 1-5 cases as in text.)

	Operation	Gestation (weeks)	Skin		Fat	
			Time*	dpm/g.	Time*	dpm/g.
Non-pregnant women	1 Tubal ligation	—	4'0"	4416	4'30"	5207
	2 Hysterectomy	—	2'0"	2126	2'10"	13 336
Pregnant women	3 Pregnant hysterectomy	15	3'20"	4529	3'25"	0
	4 Hysterotomy and tubal ligation	19	6'5"	2591	7'0"	1703
	5 Hysterotomy and tubal ligation	16	2'0"	2137	2'10"	4319

* Times quoted (in minutes and seconds) refer to time intervals from injection to removal of tissue.

than 5 per cent of the radioactivity was detected in the faeces from each patient.

DISCUSSION

This study has revealed no difference in the distribution or elimination of $9\text{-H}^3\text{-PGF}_{2\alpha}$ in pregnant and non-pregnant women. After injection of $9\text{-H}^3\text{-PGF}_{2\alpha}$ nearly all the radioactivity disappeared from the circulation within 20 minutes. Distribution of the radioactivity occurred evenly throughout a variety of tissues and no selective uptake by the uterus was demonstrated. These results differ from those of autoradiographic studies performed in female mice and rats which demonstrated a small uptake of radioactive material by the uterus about 20

minutes after injection of $\text{H}^3\text{-PGE}_1$ (Horton, 1972).

In this study excretion of the radioactivity was extremely rapid and virtually complete within 24 hours. These results are in keeping with those of Granström and Samuelsson (1971a, 1971b), who found that the excretion of radioactive metabolites following injection of $9\text{-H}^3\text{-PGF}_{2\alpha}$ was complete within seven hours.

The concentrations of radioactivity found in fetal tissues during this study indicate that placental transfer of $\text{PGF}_{2\alpha}$ or its radioactive metabolites occurs freely, as might be expected with a low molecular weight compound. The high levels of radioactivity found in the fetal liver, rather than in the fetal lungs, probably

TABLE II
Levels of H^3 (dpm/g.) in fetal tissues

Case	Time after injection of removal of fetus and placenta (minutes and seconds)	Liquor	Umbilicus	Placenta	Cord blood	Skin	Liver	Lung
3	20'25"	2924	806	2434	536	1567	12 441	1426
4	19'20"	4976	1252	1652	2552	2190	13 254	1450
5	11' 0"	660	1114	3148	1696	1079	7049	1016

teral tissues

Myometrium		Ovary		Fallopian tube		Rectus	
Time*	dpm/g.	Time*	dpm/g.	Time*	dpm/g.	Time*	dpm/g.
9'0"	6426	15'0"	3823	30'0"	5781 5388	9'30"	3154
8'50"	2376	10'30"	3380			9'0"	934
9'5"	4790	13'25"	3662			13'10"	10778
18'0"	6435	14'50"	3197			18'30"	88
11'20"	4902	6'0"	2588	19'0"	4520 4285	11'50"	1721

TABLE III
Excretion of H³ (total dpm × 10⁶) in urine and faeces

	Case	Urine					Faeces		
		1	2	3	4	Total	1	2	Total
Non-pregnant women	1	74	150	21	2.5	250	0.05	1.7	1.75
	2	Nil passed	220	14	2.7	240	0.08	1.3	1.38
Pregnant women	3	1	2	58	0.24	360	1.9	1.6	3.5
	4	300 86		140	1.2	230	2.9	1.1	4.0
	5	Nil passed	42	27	40	110	2.9	4.1	7.0

reflected a selective uptake of prostaglandin entering the liver directly via the umbilical vein and ductus venosus.

ACKNOWLEDGEMENTS

We gratefully acknowledge the help of Dr. Harrap and Mr. Coldman of the Chester Beatty Research Institute who measured the tissue radioactivity; the Upjohn Company who provided the labelled PGF_{2α}; and the M.R.C.

for their helpful interest in this work. H.C.B. was supported by an Ortho Research Fellowship administered through the R.C.O.G.

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