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PLACENTAL TRANSFER OF ALDOSTERONE IN THE GUINEA-PIG DURING LATE PREGNANCY

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SUMMARY

The rates of foeto-maternal exchange and metabolism of aldosterone were calculated from experiments in which the labeled hormone was infused at a constant rate into the maternal and foetal circulations of the guinea-pig during the last few days of intrauterine life. It was found that D-[1,2,6,7-^{3}H]-aldosterone crossed the placenta from the mother to the foetus and in the reverse direction. The maternal to foetal, as well as the foetal to maternal ratios of the tracer, increased between 60 and 67 days of gestation. The maternal contribution to the concentration of aldosterone in the plasma of the foetus was of 23.8% at 64 days and 35.7% at 67 days. At least 60% of the aldosterone in the foetal plasma was of foetal origin. The foetus contributed very little to the concentration of aldosterone in the plasma of the mother.

INTRODUCTION

From previous studies [1] it has been shown that the concentration of aldosterone in the plasma of the near-term pregnant guinea-pig was always higher than that of the foetus. The ratio of maternal to foetal plasma ranged from 9 at 62 days to 3 at 64 days and to 1.6 at 67 days of gestation. On the other hand, the concentration of aldosterone in the plasma of the foetus increased in parallel with the adrenal aldosterone content between 62 and 67 days of gestation, so that aldosterone in the plasma of the foetus might only originate from the foetus. Therefore it was of interest to know what portion of plasma aldosterone in the foetal compartment was derived from the maternal side and also what portion of the foetal plasma aldosterone was transferred to the maternal compartment. The purpose of this article is to present results obtained from experiments in which labeled aldosterone was infused at a constant rate into the foetal and maternal circulations of the guinea-pig. The rates of foeto-maternal exchange and metabolism of aldosterone can be estimated from the concentration of the labeled compound in blood at the isotopic steady state during infusion of the tracer.

MATERIALS AND METHODS

Animals. Pregnant guinea-pigs (Dunkin–Hartley strain) were used in all experiments. The adult females (700–800 g) were caged with the males for 24 h during oestrus when vaginal opening occurred. The date of conception was established with an error of ±12 h and duration of pregnancy of the studied strain was 68 days. The guinea pigs were given tap water *ad libitum*, and fed a complete cereal ("Aliment complet U.A.R."). The food intake was 40.5 ± 2.3 (S.E.M.) g/day which corresponds to 12 mEq potassium and 6 mEq sodium daily.

In a first experiment seven pregnant guinea-pigs (60 days of gestation) and their foetuses (removed by Caesarean section) were killed by decapitation. The blood taken from the neck was centrifuged and the plasma and adrenals were frozen at −20°C. The concentrations of aldosterone in the plasma and the adrenal glands were determined by radioimmunoassay, as previously described [1].

In a second experiment, three groups of pregnant guinea-pigs: 60 days (8), 64 days (6), 67 days (6) were anesthetized with sodium pentobarbital, injected intraperitoneally, (35 mg/kg body weight) and atropin (0.25 mg/kg body weight). Catheters were placed into the maternal left common carotid artery and the right external jugular vein. Chromatographically purified D-[1,2,6,7-^{3}H]-aldosterone was infused at a constant rate via the jugular vein.

In a third experiment, three groups of pregnant guinea-pigs: 60 days (5), 64 days (5), 67 days (7) were anesthetized as previously described. A catheter was placed into the maternal left common carotid artery. One uterine horn was exposed through a midline incision and a foetus was then located by palpation. The fore-limbs of the foetus were brought through a small incision in the uterus and membranes, with preservation of the amniotic fluid. The umbilical cord was intact and as far as possible exposed surfaces were covered with wet and warm cotton wool and plastic sheeting. Catheters were inserted into the right

common carotid artery and the left external jugular vein. Chromatographically purified D-[1,2,6,7-^{3}H]-aldosterone was infused at a constant rate via the jugular vein of the foetus.

Preparation of the infusate. D-[1,2,6,7-^{3}H]-aldosterone (80–105 Ci/mmol) was obtained from New England Nuclear. Radiochemical purity was established by paper chromatography using the solvent systems: (a) chloroform–formamide; (b) isooctane–butanol ter–water (2:1:1, by vol.) and after oxidation with periodate by thin layer chromatography using a benzene–acetone (3:1, V/V) solvent system. According to the above criteria the radiochemical purity of the steroid was verified by adding 15 μg carrier aldosterone to a small portion of the radioactive steroid and separation by paper chromatography using the Bush B5 system as the developing solvent. In every case the radioactivity migrated with the standard and when scanned by a Packard Radiochromatogram Scanner appeared as a single peak. The tracer steroid was dissolved in a 5% glucose solution in a concentration that was equivalent to 10×10^6 d.p.m./ml.

Infusion procedures. The solutions to be infused into the mother (second experiment) and into the foetus (third experiment) were placed into 5-ml syringes mounted on a constant infusion pump (B-Braun Melsungen) set to deliver 0.62 ml/h into the mother and 0.25 ml/h into the foetus. In the second experiment, four blood samples (0.3 ml each) were drawn in heparinized syringes from the carotid artery of the mother at 10 min intervals, beginning 90 min after the start of the experiment. In the third experiment four blood samples were drawn in heparinized syringes from the carotid artery of the foetus (0.1 ml each) at 10 min intervals, beginning 85 min after the start of the infusion and four blood samples were drawn from the carotid artery of the mother (0.5 ml each) in heparinized syringes at 10 min intervals, beginning 90 min after the start of the experiment. The rates of D-[1,2,6,7-^{3}H]-aldosterone infusions were determined by collecting three 10 min effluxes from the constant infusion pump.

Analysis of plasma labeled aldosterone. In the second experiment we managed to insert catheters into the carotid artery of one of the foetuses at every stage (60, 64 and 57 days of gestation) and collect blood samples (0.1 ml each) at 10 min intervals, beginning 85 min after the start of the experiment, but the amount of labeled aldosterone in every 0.1 ml sample was so low that it was impossible to take it into account. We therefore removed the foetuses by Caesarean section at the end of the tracer infusion experiment, killed them by decapitation, collected blood from the neck and determined the labeled aldosterone in the whole plasma. In the third experiment labeled aldosterone was analysed in every sample drawn from the foetus and from the mother.

After centrifugation and plasma separation, the maternal and foetal samples were frozen at −25°C until analyzed. After the addition of 15 μg of non-radioactive aldosterone (11β, 21-dihydroxy-6-pregnene-3,20-dione-18-al, Sigma Chemical Company) and 1.0 ml of water, the diluted plasmas were extracted three times with 5 ml of dichloromethane at 0 C. The dichloromethane extracts were combined, concentrated under nitrogen and chromatographed on paper using the Bush B5 solvent system. Each sample was eluted with methanol, concentrated under nitrogen and counted in a Packard Scintillation analyser for 30 min. Statistical analysis of the data was performed utilizing Students' *t*-test.

Parameters of metabolism and foetoplacental transfer of aldosterone. The various parameters in Table 4 were calculated by the formulas given by Gurpide[2] and are defined as follows: (1) Metabolic clearance rate (MCR), defined as the ratio of infusion (d.p.m./min) and the concentration of aldosterone radioactivity in the circulation into which it was infused, MCRm for the mother and MCRf for the foetus. (2) Blood production rates (BPRm for the mother and BPRf for the foetus), defined as the product of the MCR and the endogenous concentration of the hormone in that compartment. (3) Qm and Qf defined as the mean aldosterone secretion rates of the maternal and foetal adrenals. (4) Vfm and Vmf defined as the rates at which aldosterone is transferred from the mother to the foetus and in the reverse direction. (5) Vf defined as the rate by which aldosterone is irreversibly removed from the foetal circulation before appearing in the maternal circulation and Vm applies to all processes by which aldosterone leaves the circulation of the mother before appearing in the foetus. (6) ΔFM defined as the fraction of the total aldosterone in the plasma of the mother which is derived from the foetal adrenals and ΔMF defined as the corresponding fraction of the total aldosterone in the plasma of the foetus which is derived from the adrenal glands of the mother.

The concentrations of aldosterone in the plasma of the mothers and the foetuses were determined in animals different from those infused with labelled aldosterone. Concentrations of aldosterone in the plasma of the 64 and 67 day mothers and foetuses were taken from our previous study [1], except for 60-day mothers and foetuses.

RESULTS

Concentration of aldosterone in the maternal plasma and concentration of aldosterone in the foetal plasma and adrenal glands at 60 days of gestation

The maternal plasma aldosterone level at 60 days was high when compared to that of the 64-day mothers but was similar to that of the 67-day mothers (Table 4). Aldosterone could not be detected in the plasma of the 64 and 67 day mothers and foetuses were taken from our previous study [1], except for 62-day foetuses (Table 1).

Parameters of metabolism of aldosterone in the pregnant guinea-pig and the foetus at the end of gestation

As can be seen in Table 4 various parameters could not be determined in the 60-day mothers and foetuses since the concentration of aldosterone in the foetal compartment was not detectable at this stage.

Metabolic clearance rates (MCRm, MCRf). The MCRm and MCRf values (liters/day) rose gradually from 60 up to 67 days (Table 4). The MCRm value (liters/day) was significantly greater for the 67-day mothers than for the 60-day mothers ($0.01 < P < 0.02$), as was the MCRf value (liters/day) at 67 days compared to that of the 60 days. When expressed as liters/day/100 g body weight there were no significant changes.

Blood production rates (BPRm: BPRf). It can be seen from Table 4 that the BPRm (μg/day) was the same at 60 and 67 days. The BPRf value was significantly higher at 67 than at 64 days ($P < 0.001$).

Aldosterone secretion rates of the adrenals (Qm, Qf). The Qm and Qf values rose from 64 to 67 days. The difference between the Qm values at 64 and 67 days as well as the difference between the Qf values at 64 and 67 days was statistically significant ($P < 0.001$).

Irreversibly removal rates (Vm, Vf). The Vm and Vf values rose from 64 to 67 days. The Vm values as well as the Vf values were significantly higher at 67 than at 64 days ($P < 0.001$).

Placental transfer of aldosterone

As can be seen from Tables 2, 3 and 4 there was a passage of D-[1,2,6,7-^{3}H]-aldosterone from the mother to the foetus and in the reverse direction. The foetal plasma level of the tracer expressed as percentage of the maternal value rose gradually from 60 to 67 days (Table 2). The difference between the 60- and 67-day values was statistically significant, as was that between the 64- and 67-day values ($P < 0.001$). The maternal plasma level of the labelled hormone expressed as percentage of the foetal value increased from 60 to 67 days (Table 3). The difference between the 60- and 67-day values was statistically significant ($P < 0.001$) as well as that between the 64- and 67-day values ($0.001 < P < 0.01$).

Table 4 shows that while the total aldosterone in the plasma of the mother derived from the foetal adrenals increased significantly from 6.5 to 19.4% between 64 and 67 days ($P < 0.001$), the total aldosterone in the plasma of the foetus derived from the maternal adrenals did not change.

Table 1. Concentration of aldosterone in the plasma of the mother and concentration of aldosterone in the plasma and adrenal glands of the foetus in the guinea-pig at 60 days of gestation

Pregnant guinea-pig	Maternal haematocrit (%)	Maternal plasma aldosterone (pg/ml)	Foetuses	Foetal haematocrit (%)	Foetal plasma aldosterone (pg/ml)	Foetal adrenal aldosterone (ng/100 mg adrenal gland)
			F1 115	—	N.D.	—
115	41	446.7	F2 115	—	N.D.	—
			F3 115	50	—	—
			F1 146	51	N.D.	1.0
146	41	381.0	F2 146	51	N.D.	N.D.
			F3 146	50	N.D.	—
			F4 146	50	N.D.	3.3
			F1 440	55	N.D.	N.D.
440	30	705.0	F2 440	51	N.D.	1.4
			F3 440	52	N.D.	N.D.
			F4 440	50	N.D.	2.3
			F1 1264	53	N.D.	1.2
1264	40	539.0	F2 1264	52	N.D.	1.7
			F3 1264	51	N.D.	1.3
			F1 1281	50	N.D.	6.4*
1281	42	480.4	F2 1281	—	N.D.	11.4*
			F3 1281	—	N.D.	9.6*
			F1 1287	53	N.D.	N.D.
1287	40	335.0	F2 1287	53	N.D.	0.8
			F3 1287	50	N.D.	0.4
			F1 1291	—	N.D.	2.3
1291	35	581.7	F2 1291	—	N.D.	2.0
			F3 1291	—	N.D.	2.3
Mean ± S.E.M.	38.4 ± 1.6	495.5 ± 47.5		51.4 ± 0.4		1.3 ± 0.3

Foetal adrenal aldosterone (μg/100 mg adrenal gland) in the 62-day foetuses: 1.2 ± 0.3. N.D.: not detectable. Sensitivity of the radioimmunological method: 10 pg. * These numerals were discarded.

Table 2. Plasma concentration of D-[1.2.6.7-^{3}H]-aldosterone at steady state in the pregnant and foetal guinea-pig at the end of gestation (mother infused)

Gestation (days)*	Guinea-pig No.	Plasma D-[1.2.6.7-^{3}H]-aldosterone Mother 90 min	100 min	110 min	120 min	Mean†	Foetus* Mean†	Rate of infusion (d.p.m./min)	Foetal/maternal × 100
	8	5647.0	5407.0	5456.8	—	4568.7	44.1	120462	1.0
	11	6480.0	5979.0	6107.0	6352.0	5749.7	54.3	108344	0.9
	25	6256.0	—	6004.6	6031.3	7038.9	149.5	86623	2.1
	27	8139.0	—	8597.0	8470.0	6309.0	133.7	133176	2.1
60	282	—	7402.0	7234.0	7458.0	6695.9	—	109989	—
	293	4097.0	4093.0	4127.0	3818.0	4710.3	—	85637	—
	331	6933.0	6607.0	6614.0	6287.0	6365.9	—	103838	—
	435	4454.6	4004.0	4135.3	3908.0	4723.5	231.3	87340	4.9
	Mean + S.E.M.								2.2 ± 0.4
	4	4366.6	4140.0	4602.0	4144.0	5043.7	348.0	85516	6.9
	5	2940.6	3381.1	2820.1	3335.8	4518.6	963.7	69034	21.3
64	192	2919.3	3226.7	3048.7	2676.7	4908.2	349.6	60468	7.1
	405	3874.5	3570.0	4267.3	3874.5	5066.3	286.8	76912	5.7
	407	3625.0	3541.0	4031.2	3397.1	4992.4	560.0	73083	11.2
	429	4272.5	4201.7	4309.0	—	5449.6	454.0	78189	8.3
	Mean ± S.E.M.								10.1‡ ± 1.5
	38	3840.0	3035.0	4228.0	3702.0	5282.2	906.0	70069	17.2
	195	4195.0	3412.0	4460.0	4051.0	3756.9	1185.6	107256	31.6
67	421	—	3778.7	3550.1	3705.2	4864.2	489.1	75614	10.1
	430	3162.5	3152.5	3305.0	3295.5	4695.3	1545.9	68769	32.9
	442	3775.0	4025.5	4152.9	4108.0	4986.0	526.2	80534	10.6
	468	2549.5	2562.5	2825.5	2462.1	4387.1	948.8	59263	21.6
	Mean ± S.E.M.								20.6§ ± 2.2

* Three or four foetuses for each mother. † Mean/10^5 d.p.m./min infusion. The missing values are the result of technical errors. ‡ $P < 0.001$ vs 60 days; § $P < 0.001$ vs 64 days.

Table 3. Plasma concentration of D-[1,2,6,7-^{3}H]-aldosterone at steady state in the foetus and the pregnant guinea-pig at the end of gestation (foetus infused)

Gestation (days)	Guinea-pig No.	Plasma D-[1,2,6,7-^{3}H]-aldosterone (d.p.m./ml)										Rate of infusion (d.p.m./min)	Maternal/foetal × 100
		Foetus					Mother						
		85 min	95 min	105 min	115 min	Mean*	90 min	100 min	110 min	120 min	Mean*		
60	535	12008.0	11590.6	13175.3	12820.0	12266.1	917.4	1078.9	942.7	—	969.2	101080	7.9
	610	6632.0	6014.5	6896.5	7089.0	9652.1	537.3	598.9	584.5	610.8	845.0	68980	8.8
	613	7505.3	7878.5	7498.0	6919.0	10223.3	768.0	726.6	770.6	860.6	1072.4	72875	10.5
	618	8609.5	8544.9	9005.3	8064.6	10440.3	—	607.0	564.7	614.7	726.6	81953	7.0
	782	6536.3	6236.4	6228.2	6434.5	11154.5	612.7	—	584.2	626.3	1041.4	58352	9.3
	Mean ± S.E.M.												8.7 ± 0.6
64	612	7536.3	6620.6	8066.0	7184.0	8535.8	—	1090.3	995.3	1025.0	1214.8	86128	14.2
	624	5914.5	5955.6	6274.0	6091.3	7354.4	1500.2	—	1414.3	1400.5	1745.8	82385	23.7
	629	5116.0	5238.7	4712.0	5105.0	7161.1	665.5	717.3	726.3	721.7	1003.0	70560	14.0
	704	7347.5	7536.7	7136.2	7439.4	8628.0	1256.3	1132.2	1333.2	1281.5	1465.4	85362	17.0
	810	11095.2	10184.7	9163.3	11372.2	10456.9	1474.3	1273.3	1328.6	1457.8	1383.9	99971	13.2
	Mean ± S.E.M.												16.4 ± 1.9
67	485	8621.3	8687.5	8095.2	8482.0	9041.3	2124.9	1829.0	1997.7	2176.6	2168.8	93698	24.0
	518	5494.0	6363.0	5203.0	6048.0	5737.2	1823.8	1707.1	1763.0	1774.9	1755.0	100693	30.6
	527	8303.5	8143.5	8108.0	8287.0	8013.0	1568.5	1726.2	1582.6	—	1586.7	102466	19.8
	537	5437.4	5878.8	5343.5	5870.8	5366.3	1843.5	1885.4	1795.6	1843.8	1755.0	104963	32.7
	625	5945.0	6136.6	5876.0	6534.5	8347.0	2270.3	2150.3	2178.3	2273.8	3015.9	73547	36.1
	640	5543.5	5827.5	5572.0	6314.5	8880.0	2576.5	2674.6	2730.2	2772.3	4105.8	65478	46.2
	720	8453.7	8721.2	8246.4	8547.8	8126.4	2154.3	2236.3	2042.7	2352.8	2109.0	104502	26.0
	Mean ± S.E.M.												30.8 ± 3.3

* Mean/10^5 d.p.m./min infusion. The missing values are the result of technical errors. † $P < 0.01$ vs 60 days; ‡ $P < 0.01$ vs 64 days.

Table 4. Maternal–foetal dynamics in the guinea-pig at the end of gestation

Parameters	Gestation (days) 60	64	67	P
PACm (pg/ml)	495.5 ± 47.5 (n = 7)	284.8* ± 28.8 (n = 17)	419.3† ± 44.4 (n = 16)	*P < 0.001 †P < 0.001
PACf (pg/ml)	N.D. (n = 22)	113.8 ± 24.2 (n = 20)	263.5† ± 54.0 (n = 25)	*P < 0.001
MCRm (l/24 h)	25.6 ± 1.6 (n = 8)	28.9 ± 0.7 (n = 6)	31.3‡ ± 1.6 (n = 6)	‡P < 0.02
MCRf (l/24 h)	13.5 ± 0.5 (n = 5)	17.4* ± 1.1 (n = 5)	19.6† ± 1.7 (n = 7)	*P < 0.02 †P < 0.02
MCRm (l/24 h/100 g body weight)	2.1 ± 0.2 (n = 8)	2.2 ± 0.6 (n = 6)	2.4 ± 1.7 (n = 6)	N.S.
MCRf (l/24 h/100 g body weight)	1.9 ± 0.2 (n = 5)	2.1 ± 0.2 (n = 5)	2.0 ± 0.2 (n = 7)	N.S.
BPRm (μg/24 h)	12.2 ± 0.8 (n = 8)	8.2* ± 0.2 (n = 6)	13.1† ± 0.7 (n = 6)	*P < 0.01 †P < 0.01
BPRf (μg/24 h)	—	2.0 ± 0.1 (n = 5)	5.2† ± 0.2 (n = 7)	†P < 0.001
Qm (μg/24 h)	—	7.5 ± 0.9 (n = 11)	11.4† ± 0.3 (n = 13)	†P < 0.001
Qf (μg/24 h)	—	1.4 ± 0.1 (n = 11)	3.6† ± 0.2 (n = 13)	†P < 0.001
Vm (μg/24 h)	—	7.5 ± 0.1 (n = 11)	12.1† ± 0.2 (n = 13)	†P < 0.001
Vf (μg/24 h)	—	1.5 ± 0.1 (n = 11)	2.8† ± 0.2 (n = 13)	†P < 0.001
Vmf (μg/24 h)	—	0.5 ± 0.04 (n = 11)	2.0† ± 0.2 (n = 13)	†P < 0.001
Vfm (μg/24 h)	—	0.5 ± 0.02 (n = 11)	2.8† ± 0.1 (n = 13)	†P < 0.001
ΔFM	—	0.065 ± 0.01 (n = 11)	0.194† ± 0.02 (n = 13)	†P < 0.001
ΔMF	—	0.238 ± 0.08 (n = 11)	0.357† ± 0.08 (n = 13)	N.S.

PACm: plasma aldosterone concentration in the mother; PACf: plasma concentration in the foetus. All the other parameters are defined in the text under Materials and Methods. The results are expressed as mean ± S.E.M. N.D. not detectable. * Pvs 60 days; † Pvs 64 days; ‡ Pvs 60 days. N.S. non significant.

DISCUSSION

Aldosterone in the 60 days foetuses

Aldosterone is biosynthetized in the foetal adrenal glands of various species such as man [3, 4, 5], sheep [6] and guinea-pig [1, 7]. It is to be noted that although we find aldosterone in the foetal adrenal gland at 60 days of gestation, the adrenal aldosterone content is very low when compared to that of the 64-, 66- or 67-day foetuses [1]. The most striking fact is the lack of aldosterone in the foetal plasma at 60 days of gestation; the maternal aldosterone, at this stage, crosses the placenta in such an amount (Table 4) that it is below the sensitivity of the radioimmunological method used to determine the plasma aldosterone concentration.

Parameters of metabolism of aldosterone in the pregnant guinea-pig and the foetus during the last days of intrauterine life

The parameters calculated in this study are to have some physiological significance if we assume that the biological system under study is in the steady state. Because of the conditions of our study, it was impossible to obtain, in the second experiment, more than a sample of foetal blood. Therefore we cannot prove that D-[1,2,6,7-^{3}H]-aldosterone had reached a steady state in the foetal compartment. However, the data in Table 3 shows that the steady state is reached, in the foetus and the mother, at the same time when the foetus is infused with the tracer. Another assumption is that the labelled and the endogenous hormone entering the circulation have an identical metabolic fate. This assumption seems reasonable in the maternal and foetal circulations since labeled aldosterone infused into the external jugular vein of the mother and the foetus is rapidly mixed with endogenous aldosterone in the right heart.

The metabolic clearance rates MCRm and MCRf expressed as liters/day increase in parallel from 60 to 67 days. This is in relation with an increase in body weight since these parameters do not change when expressed as liters/day/100 g body weight (Table 3). However the MCR (liters/day/100 g body

weight) in the pregnant guinea-pig is higher than that of the non-pregnant female [8].

For all other parameters calculated in this study it should be born in mind that the concentrations of aldosterone in the maternal and foetal plasma were determined in animals different from those infused with labelled aldosterone. However, there is no other way to determine the concentration of aldosterone in the mother and in the foetus, the plasma samples drawn from the mother or from the foetus being too low to measure aldosterone, even by radioimmunoassay.

Placental transfer of aldosterone

Our findings demonstrate that D-[1,2,6,7-^{3}H]-aldosterone crosses the placenta from the mother to the foetus and in the reverse direction. Bayard *et al.*[9] have shown that, in the pregnant woman at the end of pregnancy, the aldosterone produced by the maternal compartment is transferred to the foetus. Such a transfer occurs in the pregnant guinea-pig at 30–40 days of gestation [7], the percentage of radioactivity transferred to the foetus, at the stage, is very low. This, together with our results from the 60-day foetuses indicate that there is a little materno–foetal transfer of aldosterone in the guinea-pig until 60 days. At every stage (60, 64 and 67 days of gestation) the tracer concentration is higher in the compartment in which it is infused than in the other compartment. This could be due to a high metabolism of aldosterone by the placenta of the guinea-pig so that the amount of aldosterone entering the compartment on the other side is very low. The recent work by Pasqualini *et al.*[10] supports this hypothesis since they have shown that aldosterone is largely metabolysed in the different foetal tissues and placenta of the guinea-pig at 35–45 days of gestation. Furthermore, the fact that the maternal to foetal ratios are always higher than the foetal to maternal ratios indicates that a portion of D-[1,2,6,7-^{3}H]-aldosterone infused into the mother and entering the foetal circulation never reaches the right heart since a considerable amount of the umbilical vein blood coming from the placenta does not go directly to the inferior vena cava via the ductus venosus but is subjected to metabolism by the liver parenchyma. The increase in the foetal to maternal and the maternal to foetal ratios in the last few days of pregnancy could be related to the quantitative changes observed in the haemomonochorial placenta of the guinea-pig during late gestation [11]. The foetus contributes very little to the total concentration of aldosterone in the plasma of the mother since only 6.5% at 64 days and 13.4% at 67 days of the hormone in the maternal compartment originate from the foetal adrenals. Although the maternal contribution to the concentration of aldosterone in the plasma of the foetus is of 23.8% at 64 days and 35.7% at 67 days, at least 60% of the aldosterone in the foetal plasma is of foetal origin. This is good agreement with the study of Bayard and Boulard[12] who found that, at the end of pregnancy, the human foetus secretes 80% of the aldosterone measured in the foetal compartment.

The present study has demonstrated that both mother and foetus secrete aldosterone and therefore represent two pools with secretion and metabolism in both. At 60 days of gestation there is a relative resistance to aldosterone crossover from the maternal to the foetal side. The placental barrier enables the foetus to maintain a lower concentration of aldosterone than its mother and thus to insure an independant homeostatic regulation of its level.

REFERENCES

1. Giry J. and Delost P.: Changes in the concentration of aldosterone in the plasma and adrenal glands of the foetus, the newborn and the pregnant guinea-pig during the perinatal period. *Acta endocr., Copenh.* **84** (1977) 133–141.
2. Gurpide E.: Mathematical analysis for the interpretation of *in vivo* tracer infusion experiments. *Acta endocr., Copenh. Suppl.* **158** (1972) 26–43.
3. Longchamp J.: In *Hormonologie de la grossesse humaine* (Edited by M. F. Jayle). *Monographie Rev. Eur. Endocrin.* Gauthier Villars, Paris (1965) pp. 205–218.
4. Pasqualini J. R., Wiqvist N. and Diczfaluzy E.: Biosynthesis of aldosterone by human foetuses perfused with corticosterone at mid-term. *Biochim. biophys. Acta* **121** (1966) 430–431.
5. Dufau M. L. and Villee D. B.: Aldosterone biosynthesis by human fetal adrenal *in vitro*. *Biochim. biophys. Acta* **176** (1969) 637–640.
6. Wintour E. M., Brown E. H., Denton D. A., Hardy K. J., McDougall J. G., Oddie C. J. and Whipp G. T.: The ontogeny and regulation of corticosteroid secretion by the ovine foetal adrenal. *Acta endocr., Copenh.* **79** (1975) 301–316.
7. Pasqualini J. R., Sumida C. and Gelly C.: Mineralocorticoid receptors in the foetal compartment. *J. steroid Biochem.* **3** (1972) 543–556.
8. Khaldoun T., Giry J. and Delost P.: Concentration plasmatique et taux de clairance métabolique de l'aldostérone chez le cobaye, au sevrage, à la puberté et à l'âge adulte. *C.r. Soc. Biol.* **171** (1977) 784–790.
9. Bayard F., Ances I. G., Tapper A. J., Weldon V. V., Kowarsky A. and Migeon C. J.: Transplacental passage and fetal secretion of aldosterone. *J. clin. Invest.* **49** (1970) 1389–1393.
10. Pasqualini J. R., Bedin M. and Cogneville M.: Transformation of [1,2-^{3}H]-aldosterone in the foetal and placental compartments of the guinea-pig. *Acta endocr., Copenh.* **82** (1976) 831–841.
11. Firth J. A. and Farr A.: Structural features and quantitative age-dependent changes in the intravascular barrier of the guinea-pig haemochorial placenta. *Cell Tiss. Res.* **184** (1977) 507–516.
12. Bayard F. et Boulard C.: La sécrétion d'aldostérone chez le foetus et le nouveau-né. In *Hormones et régulations métaboliques.* Masson et Cie, Paris (1973) pp. 35–42.