281 ALANINE PRODUCTION FROM THE IN VITRO HUMAN PLACENTA. Anthony F. Philipps, Joseph W. Dubin, and Paul J. Matty (Spon. by Robert H. McLean) University of Connecticut Health Center, Dept. of Pediatrics, Farmington, CT.

The ability of the human placenta to transport amino acids from the mother to fetus is well documented. Net synthesis of certain amino acids such as alanine (A) via transamination is known to occur in such tissues as muscle but it is unclear whether this capacity is shared by placental tissue. Five human placentas were obtained after elective caesarean section. Placental fragments were incubated in a bicarbonate-buffered Earle's solution enriched with oxygen. Placental A production was assessed during a 45 min incubation period by observing the net change in A in tissue and media before and after incubation. Placental glucose (G) consumption was measured utilizing a similar method. Net placental A production was 0.42±0.10 μmoles/gm wet weight/45 min ($p<.01$). When adjusted for total placental and fetal weights a net placental production of 1.56±0.34 μmoles/kg fetus/min is evident. This represents approximately 1/3 of the A uptake in the fetal sheep. Placental G consumption varied between placentas (mean 4.54±0.78 μmoles/gm/45 min) but was not related to A production. Neither the addition of pyruvate nor insulin altered A production or G consumption. Incubations of 15, 30 and 45 minutes revealed a linear relationship between incubation time and A production, evidence against a simple leaching phenomenon. These data suggest the possibility of intraplacental nitrogen transfer with net synthesis of alanine, a potential fetal fuel as well as protein constituent.

282 MATURITY RELATED DIFFERENCE IN CEREBRAL PERFUSION PRESSURE (CPP) CHANGES SECONDARY TO HYPOXIA IN PUPPIES. Tonse N.K. Raju, Rama Bhat, Dharmapuri Vidyasagar. University of Illinois, Department of Pediatrics, Chicago.

Changes in CPP (mean BP-ICP) to hypoxia were studied in 16 puppies of two age groups: Group I, 9 older puppies, $\bar{x}$ age 26 days, and Group II, 7 young puppies, $\bar{x}$ age 11 days. Mean aortic BP, heart rate, respiration and ICP (via epidural space) were recorded while 5-10% O_2 breathing. The table shows results (BP, pO_2, ICP, CPP are Torr). Within seconds of breathing low conc. of O_2, ICP rose in

	Baseline		Δ % Following Hypoxia							
			1 min.		3 min.		4 min.		5 min.	
	Gr.I	Gr.II	Gr.I	Gr.II	Gr.I	Gr.II	Gr.I	Gr.II	Gr.I	Gr.II
pO_2	60.7	70	-44%	-78%					-78%	-68%
ICP	9	9.5	+87%	+74%	+102%	+121%	+56%	+83%	+30%	+74%
CPP	64	56	-28%	-4%	-30%	-14%	-48%	-18%	-50%	-10%
BP	72	62	-17%	+5%	-18%	+3%	-37%	+5%	-40%	+3%

all animals. In Group I hypotension occurred by 1 min., persisting up to 5 min., thus resulting in severe drop of CPP ($p<0.01$). In Group II, ICP rose ($p<0.01$) but CPP drop was not significant up to 3 min. since these animals maintained BP during hypoxia. In both groups CPP dropped 5 mins. since, by then severe bradycardia and drop in cardiac output occurred. We conclude that during hypoxia: a) In very young animals CPP drop is minimal because of hypertensive response. This might provide a 'relative' protection to the vital organ, brain; b) Increase in ICP in all animals is probably sec. to increase in cerebral blood flow; c) Prolonged severe hypoxia results in severe drop in CPP by 5 minutes.

283 METABOLISM OF PROSTAGLANDIN ENDOPEROXIDE (PGH_2) IN HUMAN NEONATAL TISSUES. Barbara Reid, Harilyn Smith, Frank Sun, Zvi Friedman, Baylor College of Medicine, Department of Pediatrics, Houston, Texas & Upjohn Research Laboratories, Kalamazoo, Michigan.

The endoperoxide PGH_2 serves as a common intermediate for the enzymatic production of prostaglandins (PG) E_2, $F_2\alpha$, thromboxane (Tx) A_2, and prostacyclin (PGI_2). These compounds have diverse physiological activities and regulate numerous functions in various tissues and organs. Therefore, the distribution of individual enzymes responsible for the bioconversion of PGH_2 into these compounds was investigated. Biopsies from lung, kidney, brain, cardiovascular system (CVS), the gastrointestinal tract (GIT), liver, pancreas and adrenal were obtained within one hour of abortion of human fetuses at 14, 16 and 21 weeks of gestation (WG). (^{14}C) PGH_2 was incubated with a microsomal fraction from each tissue homogenate. The products were isolated and identified by thin layer chromatogprahy and scintillation counting. The formation of PGE_2, $PGF_2\alpha$, TxA_2 (measured as TxB_2) and PGI_2 (measured as 6-keto $PGF_1\alpha$) in lung and kidney was demonstrated in 16 WG fetus. In addition, the formation of these compounds in the CVS and GIT was detected by 21 WG. Azo analog I inhibited biosynthesis of these compounds in duplicate incubations. The dominating pathway for PGH_2 transformation varied among tissues which frequently possesses more than one enzyme catalyzing PGH_2. The observation of PGH_2 metabolism early in gestation strongly suggests an important role for these hormones in the physiology and maturation of the human fetus.

● **284** MATERNAL-FETAL COORDINATION OF CIRCADIAN RHYTHMICITY IN THE RAT. Steven M. Reppert (Spon. by D.N. Medearis) Mass. General Hospital, Children's Service, Boston MA.

Maternal coordination of the fetal biological clock was examined. Pregnant rats were housed in diurnal lighting (LD 12:12) from mating until 2 d prior to birth when they were transferred to darkness and the pups were born and reared in darkness. Circadian output was monitored in 10-d-old pups by measuring the rhythm in pineal N-acetyltransferase (NAT) activity. Analysis of NAT in the pups revealed a large daily rhythm in activity (0.1 nmol/g/h to 20 nmol/g/h) which was coordinated by the light-dark cycle during pregnancy. To determine whether the fetus could directly perceive alterations in lighting, 2 groups of pregnant rats were raised in diurnal lighting until day 7 of pregnancy. At that time one group was blinded and both groups were subjected to a phase shift in lighting until a reversed lighting cycle (DL 12:12) was attained. All were maintained in reversed lighting from day 14 of pregnancy until 2 d prior to birth when all were placed in darkness. Analysis of NAT activity in 10-d-old pups showed that the pups from both groups of mothers exhibited a clear daily rhythm but the phase of the rhythm was 10 hrs out of phase when one group was compared to the other; the NAT rhythm for pups reared by intact mothers was synchronized by the reversed lighting cycle whereas the rhythm of the pups born to blind mothers was synchronized by the maternal lighting cycle prior to blinding. Thus, mother is essential for transmitting lighting information to the fetal biological clock. Maternal coordination appears to have evolved for the purpose of preparing the immature mammal for entry into the environment.

285 DEVELOPMENT OF THE MONOSYNAPTIC AND POLYSYNAPTIC REFLEXES IN THE CHRONIC FETAL SHEEP PREPARATION. Henrique Rigatto, Carlos Blanco, and David Walker. Dept. of Pediatrics, Univ. of Manitoba, Winnipeg, Canada and the Nuffield Institute for Medical Research, Oxford, England.

We examined the relationship between segmental spinal reflexes and electrocortical activity in fetal lambs from 105-137 days gestational age. Five fetal sheep were studied on 48 occasions. Of these, 4 were older (>120 days) and one was young (105 days onwards). Single shock stimulation (1 to 4mA; 0.1 msec duration; 0.3-0.03 Hz) was used. The mono- and polysynaptic reflexes were elicited by stimulating the sciatic nerve and recording from the peroneal or tibial nerve or vice-versa. The average latency was 3.9 msec for the monosynaptic reflex, and 22 msec for the polysynaptic reflex. In fetuses >120 days gestation both reflexes were reduced or absent in low voltage as compared to high voltage electrocortical activity. In the young fetus (105-115 days) with an undifferentiated electrocorticogram the reflexes were larger during breathing, i.e. in circumstances which correspond to low voltage electrocortical activity later in fetal life. During brief episodes of eye and breathing movements at the transition between high and low voltage electrocortical activity the reflexes were enhanced. It is tempting to speculate that the enhancement of the reflexes during increased eye and breathing movements in low voltage electrocorticogram may indicate wakefulness in utero.

● **286** MODULATION OF PLASMA ALDOSTERONE (Aldo) CONCENTRATION AND PLASMA RENIN ACTIVITY (PRA) BY ANGIOTENSIN-II (A-II) DURING FETAL LIFE. J.E. Robillard and F.G. Smith, University of Iowa, Dept Pediatrics, Iowa City, IA.

A-II was infused in 17 chronically catheterized fetal (F) lambs (116-131 days gestation) and in 7 nonpregnant adult (A) ewes. The rates of A-II infusion in F and A were adjusted to compare the effect of similar plasma A-II concentrations (pA-II) on plasma Aldo, PRA, arterial pressure (MABP); it was found that the rate of A-II infusion had to be about 5 times higher in F than in A to reach similar pA-II. The effect of A-II infusion in F and A were studied at 3 different levels of pA-II.

		C	Level I	Level II	Level III
A-II	F	81±9	141±12*	218±23*	399±27*†
pg/ml	A	43±4	128±23*	177±11*	282±17*
Aldo	F	59±14	61±15	85±20*	86±18*
pg/ml	A	49±7	148±8*	136±12*	150±11*
PRA	F	5.6±1.5	3.4±1.5*	2.5±0.7*	2.1±0.6*
ng/ml/hr	A	1.5±0.4	0.93±0.29*	0.78±0.25*	0.74±0.20*
MABP	F	44±1	47±1*	49±1*	53±1*
mmHg	A	78±3	87±2*	96±3*	104±3*

(* for $p<0.05$ when values during A-II infusion are compared to control values; † for $p<0.05$ when pA-II values in F are compared to A values.) The A-II plasma clearance rate was significantly ($p<0.001$) higher in F (179±16 ml/min/kg) than in A (40±3 ml/min/kg). The present results indicate that A-II stimulates Aldo and inhibits renin production in fetal life. It is also suggested that the responsiveness to an increased concentration of pA-II is lower in F than A.