395 HUMAN FETAL AND NEONATAL INSULIN RESPONSE TO MATERNAL HYPERGLYCEMIA AT CESAREAN SECTION (C/S). Richard M. Cowett, Yusef Barcohana, and William Oh, Brown Univ. Prog. in Med., Women & Infants Hosp., Dept. of Ped., Providence, RI

The neonatal insulin response to glucose pertubation may be blunted in the normal infant due to a stable glucose milieu in utero. We hypothesized that fetal hyperinsulinemia might be a major factor in subsequent glucose control. We evaluated fetal hyperglycemia following induced maternal hyperglycemia at C/S. Subjects included 16 non-diabetic mothers who had a repeat elective C/S under spinal anesthesia at 39.9±0.2 wks (M±SEM). All received a bolus (757±42ml) of Ringers Lactate (RL) (n=7) or RL 5% Dextrose (n=9) for 20.6±0.8 min. prior to delivery to prevent hypotension. Blood was sampled prior to infusion (MAT I) and at delivery (MAT II) and from infants via the umbilical vein (UV)and artery (UA) and for 4 hours after birth

	MEAN PLASMA GLUCOSE (mg/dl)-PLASMA INSULIN (μU/ml)						
Group	MAT-I	MAT II	UV	UA	+30	+60	+240
RL	78-17	83-18	68-16	57-14	53-15	54-17	64-14
RL+5%	82-15	286-73	219-60	158-58	86-20	63-16	71-14
p	NS-NS	.001-.001	.001-.01	.001-.01	.001-NS	NS-NS	NS-NS

All mothers and infants receiving glucose had marked hyperglycemia and hyperinsulinemia at delivery. Neonatal hyperinsulinemia subsided rapidly as plasma glucose concentration fell. No infant developed hypoglycemia after 30 min., probably related to counter-regulatory mechanisms in the newborn. We conclude that the normal term infant can respond to an exogenous glucose load with immediate elevation of plasma insulin concentration.

● 396 RISK OF RENAL DAMAGE FROM LARGE DOSE VITAMIN D THERAPY J.Curtis,A.C.Hsu, R.Baumal,C.P.Rance, B.Steele, S.W.Kooh, D.Fraser, Dept Paed., Univ of Toronto; Research Institute,The Hospital for Sick Children,Toronto,Canada.

Vit D in high dosage is a well established treatment of hypoparathyroidism (HP),pseudohypoparathyroidism (PHP), vit D dependency rickets (VDDR) and hypophosphatemic rickets (HPR). The few systematic assessments of its long-term effects on renal status have been in pts with vit D refractory rickets; some of these pts showed histological damage or functional impairment. We studied 26 pts (10 HP, 2 PHP, 6 VDDR, and 8 HPR)who received vit D or its metabolites for 1-21 (mean 11) yrs. Therapy was supervised according to a standard protocol at a special pediatric clinic, usually from the time of diagnosis. Plasma Ca was determined 2-monthly for pts on vit D or 25-OHD_3 and monthly for those on 1,25-$(OH)_2D_3$. Treatment was interrupted if plasma Ca exceeded 10.5 mg/dl and resumed with 80% of the previous dose once normocalcemia returned.The pts were normocalcemic when the studies were carried out. 7/26 had diminished GFR, 5/25 concentration defect, 1/14 acidification defect. Renal histology showed tubulointerstitial nephritis and/or calcium deposits in 17/26 pts.Eight of the pts with histological abnormalities had functional impairment; however, 2 of the 9 pts with normal histology also had functional impairment. The incidence of histological abnormalities was correlated with the duration of hypercalcemia and with diagnosis, being lowest in VDDR. These studies indicate that pts receiving large dose vit D therapy are at a high risk of sustaining histological and functional damage of the kidney.

397 URINARY GONADOTROPINS IN THE MANAGEMENT OF IDIOPATHIC PRECOCIOUS PUBERTY. Leona Cuttler, F. John Holland (Spon. by H.Bain).Hosp.Sick Child.,Dept.Peds.,Toronto.

The use of medroxyprogesterone acetate (MPA) in the treatment of idiopathic precocious puberty (IPP) is not standardized. In attempting to provide objective criteria for its use, we report the first patient in whom FSH and LH excretion rates have been measured in acid/acetone extracts of timed urine fractions sequentially before and after treatment. A 3 year old girl with IPP had enormously elevated gonadotropin excretion rates at presentation. She was treated with IM MPA 100 mg q3-4 weeks for 9 months, then p.o. MPA 5 mg q8h for 12 months. While on IM treatment, gonadotropin excretion rate fell dramatically and was associated with decreased breast size and height velocity. All these parameters increased when oral therapy was used. There have been no signs of glucocorticoid effects, hypertension, nausea, or excess weight gain. Bone age was 6 yrs 10 mos at presentation; 2 yrs later it was 8 yrs 10 mos. Although similar studies will be required in a larger number of patients, from these data we conclude that (1) sequential measurement of urinary FSH and LH excretion rates may optimize the MPA management of patients with IPP by providing objective criteria for monitoring therapeutic response (2) oral treatment,in the dosage used, is less effective than IM treatment.

	PRE-MPA	IM-MPA	PO-MPA
FSH (mIU/hr)	4883	8.6-120	>181
LH (mIU/hr)	1434	14-148	>368
height vel. (cm/yr)	16	9	11.5

398 CLEARANCE OF VASOPRESSIN BY THE FETUS AND NEWBORN. Salha S. Daniel, Raymond I. Stark, M. Kazim Husain, Ulana M. Sanocka and L. Stanley James, Div.of Perin. Med., Depts.of Ped.,Anes., & Med., Coll. of P&S, Columbia Univ., NY.

These studies were initiated in order to compare the volume and rate of distribution, the rates of metabolism and excretion of VP by the fetus to those of the newborn. Vasopressin - 2ng/kg was injected intravenously to six fetal and four neonatal lambs and VP levels were measured in sequential plasma and urine samples. Vasopressin disappeared from plasma as an exponential function composed of two components. The first phase, representing distribution, was similar in both the fetus and newborn with $T_{\frac{1}{2}}$ of 1.75 minutes. The second phase, representing excretion and metabolism, was slightly faster in the fetus than newborn, $T_{\frac{1}{2}}$ being 17 and 25 minutes respectively. Plasma concentrations extrapolated to zero time gave a volume of distribution of 285 ml/kg in the fetus and 225 ml/kg in the newborn. Data on urine concentrations show that when given as a bolus, fetal renal excretion of non-metabolized VP was minimal while in the neonate it represented 7-10% of the dose.

These results indicate that the rate of distribution of VP is essentially the same in both the fetus and newborn but the volume of distribution is slightly higher in the fetus. Despite the lack of contribution of the fetal kidney, the rate of clearance of VP is slightly faster in the fetus suggesting a role for the placenta in the metabolism of VP.

399 FACTORS IN THE RELEASE OF VASOPRESSIN BY THE FETUS DURING HYPOXIC STRESS. Salha S. Daniel, Raymond I. Stark, Alan Zubrow, Harold E. Fox, M. Kazim Husain & L. Stanley James, Div.of Perin.Med.,Depts.of Ped.,Anes.,Obs., Med., Coll. of P&S, Columbia Univ., NY.

The contribution of various factors to the release and high level of vasopressin(VP)by the fetus during hypoxic stress were examined in 27 chronically instrumented fetal lambs,118 to 135 days gestational age. They were exposed to: a)30 minutes administration of 10% O_2 to the pregnant ewe (H): b) 20 minutes partial occlusion of the umbilical cord(POC); or,c)2 minutes complete occlusion of the umbilical cord(COC). The change in fetal arterial blood pressure and plasma composition were:

	VP (pg/ml)	PO_2 (mmHg)	PH	BP (mmHg)	OSM (mOsm/kg)
H	+29.6	-9.2	0.00	+9/5	+7.0
POC	+48.3	-7.6	-0.11	+12/9	+7.9
COC	+89.6	-12.1	-0.14	+30/22	+7.9

These results indicate that osmolality is probably not a major factor in the release of VP under hypoxic stress. While hypoxemia alone does stimulate VP release, the higher VP levels following POC compared to H indicate that other factors leading to acidemia may also contribute. The rapid rise of plasma VP following 2 min. of COC during which the placental bed is temporarily excluded from the fetal circulation suggests that the placenta plays an important role in metabolism of the hormone. The large increase in BP could also be important in stimulating release of the hormone.

400 THYROXINE [T4] AND TRIIODOTHYRONINE [T3] DEPRESSION IN INFANTS EXPOSED TO PSYCHOACTIVE AGENTS IN UTERO. Shobhana Desai, Cynthia Villasis, Gary G. Carpenter, Loretta P. Finnegan. Thomas Jefferson University Hospital, Department of Pediatrics, Philadelphia, Pa.

The effects of maternal use of multiple psychoactive agents on tests of thyroid function were studied in 15 drug exposed term infants [$\bar{x}$ b.w.=2700 gms.] and compared to 15 matched healthy newborn infants [$\bar{x}$ b.w.=3120 gms.] on days 1, 4, 7, 14 and 21. On day 1, all drug exposed infants (DEI) were not receiving treatment for abstinence. During days 4 through 21, all 15 DEI were being treated with paregoric and/or phenobarbital. Serum T4 and T3 measured by CONCEPT 4 micromedic method and serum TSH measured by the CORNING method are tabulated:

	Day #1			Day #4		
	T4	T3	TSH	T4	T3	TSH
DEI	12.70	116.20	12.50	16.40	160.70	2.69
Control	18.90	256.60	26.70	18.30	187.10	7.60
p Value	<0.10	<.01	N.S.	N.S.	N.S.	<.02

Subsequent tests on days 7, 14 and 21 showed no persistent difference between DEI and controls. The possible effects of multiple psychoactive agents taken during pregnancy as well as therapeutic medications for neonatal abstinence may influence the mechanism of thyroid homeostasis before and after birth. Specifically, the enhancement of sulphydryl enzymatic activity that might stimulate β-ring diodinase, specific for 5' iodine, in effect lowering reverse T3 and increasing active thyronine (inhibiting TSH release and subsequent thyroid secretion and response) is yet to be demonstrated.