● **1171** CONTINUOUS INTRAVENOUS INSULIN DELIVERY IN AMBULATORY ADOLESCENT DIABETICS. K. Perlman, R.M. Ehrlich, R.M. Filler, and A.M. Albisser, (Spon. by D. Carver), Hosp. for Sick Child., Depts. of Peds. & Surg., Toronto, Canada.

Devices and methods for long term intravenous insulin infusion in ambulatory patients have recently been developed. With informed consent we studied 7 non-obese uncomplicated Type I diabetics (aged 15-17y) who received insulin for 14-23 days by central venous infusion (CVII). All subjects were studied in hospital with otherwise unrestricted activity and received 3 daily meals and an evening snack of constant caloric content. Under local anesthesia, a thin silicone rubber catheter was inserted into a branch of the external jugular vein, advanced to the SVC and tunnelled subcutaneously to exit in the supramammary region, where it was connected to the portable system consisting of a small peristaltic pump, a flow rate controller and a reservoir of soluble insulin. Insulin was infused at a constant basal rate of 17±3 mU/min. The rate was increased 15 minutes from the start of a meal 4-5 fold for 60-120 min then returned to the basal rate in a 2 step fashion over 40-120 min. Fasting plasma glucose (mean±SEM) was 262±40 prior to infusion and fell to 92±9 mg/dl on CVII with increases during mealtimes from 80±3 to 115±3 mg/dl at 41±3 min pc. Mean urinary glucose excretion of 55 g/day fell to 1.9 during CVII and fasting serum cholesterol of 220±28 and triglycerides of 281±94 fell to 138±13 and 115±24 mg/dl respectively. Mean HgbA1c (N:6.5 - 8.5%) fell from 14.8 to 10.7% by the end of the study period. All indices of control showed improvement with $p < 0.05$. There were no catheter related complications and the system was well accepted by all subjects. We conclude that in ambulatory adolescent diabetics continuous central venous insulin infusion without continuous glucose sensing is feasible for the prolonged normalization of glycemia and other indices of metabolic control.

● **1172** EFFECTS OF CHRONIC HYPERGLYCEMIA IN THE FETAL LAMB. Anthony F. Philipps, Joseph W. Dubin, Paul J. Matty, and John R. Raye (Spon by Arnold J. Altman) Univ. of Connecticut Hlth. Ctr., Dept. of Pediatrics, Farmington, CT.

Prolonged fetal hyperglycemia has previously been shown to cause metabolic acidosis but the mechanism involved is unclear. Chronic fetal glucose (G) infusions (mean: 8.3±2.6 d, range 3-17d) were performed in 5 fetal lambs. Infusions were varied to achieve plasma G of 2-3x basal concentration. In 4 of 5 preparations twins were used with the noninfused twin serving as internal control. Plasma G increased from 18.5±1.9 to 58.1±4.7 mg/dl during infusion. Plasma insulin (I) increased from 12±3 to 27±4 µU/ml ($p < 0.02$). Fetal arterial O_2 content (O_2) fell from 6.7±0.9 to 4.1±1.0 ml/100 ml ($p < 0.01$). Although not related to changes in I, the O_2 decrement was linearly related to the Δ plasma G from basal and, in the twins, to the difference in G between infused and control lambs ($p < 0.001$). O_2 decrement was related nonlinearly to the G infusion rate (G.I.R.) with a significant ($p < 0.01$) change noted in O_2 above G.I.R. of 10 mg/kg/min. In twins, at G.I.R. of 10-15 mg/kg/min, O_2 content of the infused twin fell to 50±15% ($p < 0.01$) of the simultaneously sampled control twin. Despite the relative hypoxemia, metabolic acidosis (base deficit >5) was not observed until $O_2 < 50\%$ control twin or G.I.R. >15 mg/kg/min. Discontinuation of infusion in 3 preparations was associated with a rise in O_2 and fall in base deficit. Amniotic (Am) fluid sampling revealed a correlation ($p < 0.01$) between plasma and Am G but not I. Chronic fetal hyperglycemia induces a relative arterial hypoxemia and hyperinsulinemia. The mechanism behind this relationship is unclear.

1173 ^{14}C -GLYCINE UPTAKE BY FIBROBLASTS IN CHILDREN WITH NONKETOTIC HYPERGLYCINEMIA. Siegfried M. Pueschel and Joan M. Boylan. (Spon. by Leo Stern). Brown University, Program in Medicine, Rhode Island Hospital, Department of Pediatrics, Providence, Rhode Island.

In the attempt to uncover underlying pathogenetic factors that bring about the biochemical aberration and the clinical symptoms observed in patients with nonketotic hyperglycinemia, investigations of glycine transport in diploid fibroblasts of children with this syndrome were initiated. Skin fibroblasts from two nonketotic hyperglycinemic cell lines and from three normal cell lines were cultured in Eagle's medium. Amino acid transport measurements were made with cells grown on sterile glass coverslips according to the method by Foster and Pardee.

The rate of ^{14}C -glycine uptake by fibroblasts from nonketotic hyperglycinemic patients did not differ from that of the control cell lines during the first part (30 min.) of the experiment, yet subsequently the rate of ^{14}C -glycine uptake decreased gradually in nonketotic hyperglycinemic cells.

The results of this study are in support of the hypothesis that glycine transport across cell membranes in patients with nonketotic hyperglycinemia is similar to the transport by the A system of other mammalian cell lines. Therefore, we do not consider the biochemical perturbation and the clinical course in nonketotic hyperglycinemia to be caused by a primary membrane transport defect.

1174 SODIUM BENZOATE THERAPY AND DIETARY CONTROL IN HYPER-ARGININEMIA. Ijaz A. Qureshi, Jacques Letarte, René Ouellet and Michel Lelièvre. Depts. of Pediatrics, Univ. of Montreal, Montreal, and Laval Univ., Quebec, Canada.

Recent reports indicate that acylation of glycine by Sodium Benzoate (SB) could be a useful mechanism for the excretion of nitrogen overload as hippurate in congenital hyperammonemias. We have treated a 16 year old French-Canadian girl, confirmed homozygote for hyperargininemia, by a 4 week SB therapy trial. During the control period (0.5g protein/kg BW diet), her fasting plasma NH_3N was 130-273 µg/dl (normal 50 ± 13), glutamine: 763-776 µg/dl (normal: 369-660) and urinary orotate: 62-516 mg/d (normal: 3 ± 1). Due to feeding difficulties, continuous intragastric infusion was started (1600 Kcal, 0.5g protein/kg), which stabilised NH_3N at 93-107, glutamine at 503-754 and orotate at 5-12.

SB (250 mg/kg BW/d), added to infusion, brought NH_3N down to 75-88, glutamine to 269-418 and orotate to < 3mg. An attempt to increase the protein intake to 0.8 g/kg was not successful, as the patient gradually developed vomiting and a hyperammonemic crisis. However, reduction of protein intake (0.25 - 0.37 g/kg) and increase in SB (333 mg/kg/d) quickly controlled the crisis. The girl was discharged after 10-day stable period on 0.5 g protein/kg BW mixed diet with oral SB. During this period her NH_3N remained at 32-48, glutamine at 252-434 and orotate at < 3 mg/d.

Measurement of urinary hippurate and partition of urinary N shows that SB therapy increases waste N excretion in hyperargininemia. On equal protein intake, hippurate N excretion increased from 2% of total N output without SB to 27% with SB.

1175 SUBSTRATE UTILIZATION IN THE GROWING VERY LOW BIRTH-WEIGHT (VLBW) FORMULA FED INFANT. Brian L. Reichman, Philippe Chessex, Guy Putet, Gaston J.E. Verellen, John M. Smith, Tibor Heim, Paul R. Swyer. Dept. Paeds. & Med. Eng., Univ. Toronto; Res. Inst., Hosp. for Sick Children, Toronto.

Nutritional needs of the growing VLBW infant are usually assessed in relation to fetal accretion rates¹. However, we show in VLBW infants differences in accretion rates from those inferred from previous studies on cadaver composition. 20 studies were performed in 13 formula fed (SMA20/24) appropriate for gestational age infants (mean±SE B.Wt: 1155±39g; study wt: 1280±70g; study age: 22±2d) to determine the rate of deposition of fat(F), carbohydrate(CHO) and protein(P). 3 day balance, indirect calorimetric and urinary N_2 studies permitted measurement of intake, losses, oxidation and deposition rates of F, CHO and P (mean±SE: g/kg.d):

	FAT	CHO	P	Kcal/kg.d
INTAKE	7.5±0.02	15.3±0.4	3.18±0.1	147.6±4.2
LOSSES(stools+urine)	1.6±0.15	0.2±0.02	0.54±0.05	19.7±1.8
OXIDATION	0.55±0.12	13.3±0.5	0.72±0.04	62.8±0.9
DEPOSITION	5.3±0.3	1.95±0.45	1.9±0.1	65.1±3.0

We conclude that in the growing VLBW infant: 1) CHO is the main energy source (85%); 2) 80% of absorbed F is stored; 3) compared to the reference fetus gaining weight comparably, F and CHO deposition is higher and P accretion is similar. This implies that the daily weight gain of the VLBW infant contains more solids(54%) (excluding minerals) than the fetus of comparable post conceptional age(23%)¹. Ref.¹ Widdowson, E.M.: In: Scientific Foundations of Paeds. pp153-163(W.B. Saunders, 1974).

1176 DIFFERENTIAL EFFECT OF PROSTAGLANDINS (PG) ON AMINO ACID (AA) TRANSPORT IN HUMAN FIBROBLASTS. Betty Revsin, Emil Stein and Richard Lemen, Arizona Health Sciences Center, Department of Pediatrics, Tucson 85724.

PGs have been implicated as agents that affect membrane transport of numerous substances, yet little is known of the role of PGs on AA membrane transport. We examined the effects of PGE₂ and PGF_{2α} on AA transport by the A, ASC and L systems. Fibroblasts were preincubated with PGE₂ or PGF_{2α} for 10 min prior to addition of the labeled AA.

	Control	PGE ₂	PGF _{2α}
Glycine*	8.3 ± 3.2**	10.7 ± 3.3***	6.2 ± 2.9***
Alanine	6.0 ± 1.5	8.1 ± 3.7	10.2 ± 3.9
Valine	4.2 ± 1.5	5.6 ± 1.6	2.9 ± 0.9
Cycloleucine	8.0 ± 3.0	11.6 ± 5.0	6.2 ± 2.3

* N = 8 using 4 cell lines for all AA's.

** mean (nmoles/100µg protein/20 min) ± S.D. ***p < 0.01

PGE₂ stimulated the uptake of all AA carrier systems while PGF_{2α} inhibited all AA transport except for alanine which has high affinity for the A system. Our studies suggest 1) PGE₂ and PGF_{2α} have opposing, dose dependent actions on the L and ASC systems (valine/cycloleucine and glycine respectively) but have the same effect on the A system (alanine) and 2) PGE₂ and PGF_{2α} may act as an autoregulatory mechanism controlling AA membrane transport in cells. Supported in part by NIH Grant HL 23773 and the Cystic Fibrosis Foundation.