†**1189** A NEW DEFECT OF β-OXIDATION: SHORT CHAIN ACYL-COA DEHYDROGENASE (SCADH) DEFICIENCY. Brad A. Amendt, Betty A. Norbeck, Anne M. Moon and William J. Rhead (Spon. by J. Robillard), University of Iowa, College of Medicine, Iowa City, Iowa.

Fibroblasts from neonate I with metabolic acidosis and ethylmalonate excretion oxidized [1-^{14}C]butyrate, -octanoate and -palmitate at 35% ($p<0.05$), 60% and 63% of control; succinate oxidation was normal. Fibroblasts incorporated ^{14}C from [1-^{14}C]-butyrate, -octanoate and -succinate into TCA insoluble material at 38% ($p<0.05$), 57% and 73% of controls. SCADH activity in fibroblast mitochondrial supernatants (MS) of neonate I was 39%, while medium chain (MCADH) and long chain (LCADH) acyl-CoA dehydrogenase (ADH) activities were 56% and 75% of control. Acetoacetyl-CoA, a SCADH inhibitor, inhibited control MS SCADH activity by 47%, while no inhibition was detected in neonate I. MS electron-transferring flavoprotein activity was 70% of control ($p=0.36$). Fibroblast sonicate (CS) SCADH and MCADH activities were 47% and 72% of control. Neonate II presented with severe metabolic acidosis, hyperammonemia, death and ethylmalonate, butyrate, adipate and lactate excretion. Dr. Vivian Shih found that this patient's fibroblasts oxidized ^{14}C-octanoate and -leucine normally, and [1-^{14}C]butyrate at 56% of control. CS SCADH and MCADH activities in neonate II were 58% and 97% of control by a dye reduction method and 53% and 95% of control using the tritium release assay. Neonate I may be a double heterozygote for both SCADH and MCADH deficiencies or possess a mutant MCADH with reduced activity toward octanoyl-CoA and no activity towards butyryl-CoA; neonate II has an isolated SCADH deficiency.

†**1190** PUBERTY AND DIABETES INDEPENDENTLY REDUCE INSULIN SENSITIVITY IN CHILDHOOD. Stephanie A. Amiel, Robert Sherwin and William V. Tamborlane. Yale Univ. School of Med., Dept. of Pediat., New Haven, CT.

The unstable metabolic control seen in adolescents with insulin dependent diabetes (IDD) is frequently attributed to psychosocial factors. To test the hypothesis that physiological changes of puberty play a role, we used the euglycemic, 1mU/kg.min insulin clamp technique (which raises plasma free insulin levels by ∿90uU/ml) to quantitate insulin sensitivity. 14 conventionally-treated, C-peptide negative IDD (5 Tanner I, 9 Tanner II-IV) and 5 Tanner I and 7 Tanner II-IV normal controls were studied. In the IDD neither the duration (7.2±1.3vs5.6±0.9yrs) nor the daily insulin dose (1.1±0.1 vs 1.0±0.1units/kg) differed between the groups (Tanner II-IV vs I). The glucose infusion rates (mg/kg.min) required to maintain euglycemia (91±0.6mg/dl) during the insulin clamp studies are shown below:

Tanner Stage	I	II-IV	
Normals	10.4±1.1	6.3±0.3*	*P<0.01 Tanner II-IV vs I
IDD	6.4±0.5[a]	3.8±0.6*[a]	[a]P<0.01 IDD vs normal

In normal children, the onset of puberty is associated with a significant reduction in insulin-mediated glucose metabolism. A further 40% reduction in insulin sensitivity is observed in IDD at each stage of development. Conclusions:1)Puberty causes a sharp reduction in insulin sensitivity in both normal and IDD children 2)IDD induces an additional defect in insulin sensitivity at each stage of development 3)The combined effects of puberty and IDD result in marked insulin resistance which may contribute to poor metabolic control in adolescent IDD.

●**1191** EFFECTS OF SALICYLATE ON OXIDATION OF OCTANOATE AND PALMITOYL COENZYME A IN RAT LIVER MITOCHONDRIA: IMPLICATIONS FOR REYE'S SYNDROME. June R. Aprille and Caroline A. Brown. Tufts Univ., Dept. Biol., Medford, MA 02155.

We studied the effect of salicylate (SA) on fatty acid (FA) oxidation in isolated rat liver mitochondria (mito), in order to investigate a possible link between the evidence for an association of aspirin ingestion with Reye's Syndrome and perturbed fat metabolism in this disease. Mito were incubated for FA oxidation with either 0.1 mM ^{14}C-octanoate (C_8) or 0.1 mM ^{14}C-palmitoyl CoA (C_{16}CoA) plus 0.5 mM carnitine as substrate. The rate of oxidation was followed as the amount of $^{14}CO_2$ formed. C_8 was chosen to represent short chain FA which are permeable to mito and which therefore can be activated to CoA esters by an ATP-dependent reaction in the matrix prior to B-oxidation. C_{16}CoA was representative of long chain FA, which are impermeable to mito and which must be activated to CoA esters in the cytosol prior to carnitine-dependent transport into the matrix for B-oxidation. SA inhibited C_8 oxidation in a concentration dependent manner with maximum inhibition (71.3±3%) at 2.5 mM SA. In contrast, C_{16}CoA oxidation was increased 49±13% by 2.5 mM SA. These effects were traced to SA's uncoupling activity, which stimulates uncoupled respiration and lowers the matrix ATP concentration. Thus at modest concentrations, SA selectively inhibits the oxidation of FA that are activated to CoA esters in the mito matrix, but stimulates the oxidation of FA that have been activated in the cytosol. This suggests a possible contributory role for aspirin in the development of Reye's Syndrome, since an excess of short chain FA has been proposed to be important in the pathogenesis of this illness. (NIH NS 14936).

1192 LYMPHOCYTE CHOLESTEROL SYNTHESIS (LCS) IN NEW ONSET IDDM PRE AND POST INSULIN THERAPY. Silva Arslanian, Vijay Warty, Sunder Suresh, Dorothy Becker, Allan Drash, University of Pittsburgh, School of Medicine, Departments of Pediatrics and Pathology, Pittsburgh, PA

LCS from C^{14} acetate was studied in freshly isolated lymphocytes in 12 ketotic children (8 females, 4 males) with new onset IDDM before (DAY 0) and 5 days after insulin therapy and in 5 controls (C) who were nondiabetic siblings of IDD. The mean age at diagnosis was 9.6 yrs. (4.6-14.8 yrs). Patients were divided according to maximum LCS into 2 groups. GP1 (n=7) maximum LCS within 3 SD of C. GP2 (n=5) maximum LCS>10 SD above C. Results were: DAY 0: maximum LCS in C, GP1, and GP2, respectively, were 440.4±45.7, 469.4±170.2, 1580.4±241.9 pmoles/hr/mg. LDL_{50}, the concentration of LDL cholesterol (ug/ml) in the medium necessary to reduce cholesterol synthesis to 50% of maximum LCS, was above 100 ug/ml in all 3 groups and higher than in adult controls (LDL_{50}<50 ug/ml). DAY 5: Post insulin therapy, maximum LCS in GP1 did not change. In GP2 it dropped significantly from that of Day 0 (530.8±520.9 vs 1580.4±241.9, $p=0.006$) and was similar to C and GP1. LDL_{50} was the same in the 3 groups and similar to Day 0. Cholesterol, LDL, VLDL, insulin, C-Peptide, glucagon, bicarbonate, triglycerides, and pH were similar in both groups, but GP1 had a significantly higher HDL and glucose level and lower B-OH butyrate than GP2 at Day 0. These results indicate that (1) abnormalities in cellular cholesterol metabolism are present in IDDM and can be corrected partly with insulin; (2) nondiabetic siblings of IDDM may have abnormal suppressibility of endogenous cholesterol synthesis with higher LDL_{50} compared to adults.

●**1193** THE UREASE INFUSED RAT AS A MODEL OF INBORN ERRORS OF UREA SYNTHESIS Mark L. Batshaw, Susan Hyman and Joseph Coyle. Dept. of Pediat., Psychiatry, Kennedy Inst. Johns Hopkins Med. Inst. Balto.

Rats treated with intravenous urease become acutely hyperammonemic (HA) and have increased tryptophan transport into the brain associated with elevated levels of serotonin and 5-hydroxy indoleacetic acid (HIAA) [Life Sciences 33; 2417, 1983]. We have implanted intraperitoneally 7 and 14 day Alzet osmotic pumps delivering 2.5 U urease/100g/24hr. Mean plasma ammonium levels were (X ± SEM) 64 ± 4 uM baseline and 392 ± 30 uM during urease infusion ($p < .01$) in 23 rats. HA lasted a mean of 8 days. Plasma amino acids showed a specific elevation in glutamine 698 ± 57 uM versus baseline 412 ± 19 uM ($p < .01$) with no alterations in branched chain amino acids or tyrosine levels as is seen in models of portal-systemic shunting. Sham operated animals showed no significant biochemical changes. In the cortex of HA animals, levels of serotonin and HIAA were increased but levels of norepinephrine, dopamine and homovanillic acid were not altered. Food intake decreased more in the HA rats than in those receiving sham surgery -6.9 ± 1.4 vs. -4.6 ± 0.9 g/d. Weight loss was also greater in the HA rats 19.8 ± 4.4 vs. 3.0 ± 1.3 g ($p < .01$). Thus behaviorally, the HA rats were anorectic, similar to children with inborn errors of urea synthesis, which suggests a relationship between altered serotonin metabolism and anorexia. The urease treated rat may prove useful in studying the neurochemical and behavioral abnormalities associated with inborn errors of urea synthesis and may permit the testing of new therapeutic approaches.

●**1194** **ABNORMAL LEFT VENTRICULAR (LV) FUNCTION IN TYPE I DIABETICS FOLLOWING MAXIMAL SUPINE EXERCISE.** Victor C. Baum, Robert A. Englander, Lynne L. Levitsky, Pritzker Sch. of Med., Univ. of Chicago, Michael Reese Hosp., Dept. of Pediatrics, Chicago, Ill.

Resting echocardiographic abnormalities have been documented in healthy young diabetics. In order to evaluate the physiologic relevance of this finding and to determine LV responses to the stress of exercise in young diabetics, 28 normal children and 30 otherwise healthy type I diabetics had M-mode echocardiograms of the LV and aorta (Ao) at rest and immediately following maximal exercise on a supine bicycle ergometer. Adequate studies were obtained in 26 controls (aged 10.7 to 17.7 yrs) and 25 diabetics (aged 9.2 to 18.3 yrs). Duration of exercise was less for diabetics (8.5±.5 vs. 7.0±.5 MIN, $p<.05$) ($\bar{x}$±S.E.). There were no significant differences in fractional shortening (FS) (.34±.01 vs. .32±.01), LV systolic time intervals (PEP/ET) (.26±.01 vs. .28±.01) or velocity of circumferential fiber shortening (Vcf) (1.17±.04 vs. 1.17±.05) at rest. Following exercise all these indices of LV contractility increased in both groups but FS was significantly different between controls and diabetics (.43±.02 vs. .37±.02, $p<.05$) as was Vcf (2.20±.12 vs. 1.77±.12, $p=.003$). 11 diabetics had finger contractures. 5 diabetics had flat septal motion at rest which persisted following exercise. All of these have had finger contractures. Otherwise healthy young diabetics have abnormal cardiac function which can be demonstrated by exercise testing with echocardiographic evaluation, a non-invasive technique. These abnormalities may relate to glycosylation of myocardial proteins. It is speculative whether they represent an early manifestation of the diabetic cardiomyopathy seen in older patients.