871 INSULIN DEPENDENT DIABETES IN WERNER'S SYNDROME-? A NEW VARIANT. Chul H. Kim, Judith V. McLaughlin, Shih-Wen Huang, Wilmer Bias, Noel K. Maclaren*. University of Maryland School of Medicine, Dept. of Pediatrics, Baltimore.

Werner's syndrome, or adult progeria, is characterized by short stature, atrophic changes in skin and muscle, sclerodermatous lesions, chronic leg ulcers, secondary hypogonadism, premature atherosclerosis, cataracts, insulin independent diabetes (I.I.D.) and an autosomal recessive inheritance. A black boy, C.M., presented at 15 years with diabetic ketoacidosis (blood sugar 848mg/dl, CO_2 6 mEq/l and 4+ acetonuria). At 17 years, he was small (4'6", 68 lbs.), looked aged, with generalized stiffness, thin taut hyperpigmented skin, a chronic leg ulcer and an insulin requirement of 50 U of NPH daily. Serum T_4 was 6.3µg/dl and growth hormone responses were normal. He had antibodies to double stranded RNA(poly A-U, 1:64) but none to DNA. His lymphocytes were cytotoxic to cultured insulinoma target cells. He had 3 adult female siblings; one with insulin dependent diabetes(I.D.D.), had presented in diabetic ketoacidosis at 19 years. At 27 years, this sister was short(4'10"), looked aged, had similar skin lesions, joint problems and premature menopause. The remaining 2 sisters were unaffected(5'7", 5'10"). Mother,had I.D.D.with skin and joint problems, died at 48 years of a stroke. Of her 7 siblings,2 had I.I.D., while 2 others died of strokes at 42 and 52 years. These cases have clinical similarities with Werner's syndrome,however, I.D.D.,early presentation, and probable autosomal dominance as supported by histocompatibility antigen typing,are novel features.

872 A NEW FORM OF CONGENITAL LACTIC ACIDOSIS. Jeffrey J. Kline, Ted D. Groshong, David O. Quissell, Lawrence Sweetman, William Nyhan, Yasuhiro Kuroda, and George Hug. University of Missouri, Columbia, Missouri, University of California-San Diego, San Diego, California and University of Cincinnati, Cincinnati, Ohio.

Two siblings, 6 and 40 months of age, with a previously unrecognized form of pyruvate decaboxylase (PDC) developed lactic acidosis, hyperammonemia, and proximal renal tubular acidosis, along with persistent ketosis and severe retardation of growth and development. Urine metabolites showed consistently high lactate, pyruvate, fumarate, and succinate, the latter two unusual in most forms of congenital lactic acidosis. Ornithine transcarbmyalase was demonstrated at 50% normal activity in the one patient measured. This may partially explain the persistent hyperammonemia. Therapy with megadoses of thiamine, pyridoxine, and monosodium glutamate were without effect. Large doses of biotin caused a transient decrease in the lactic acidosis but no long term clinical effect was demonstrated. Ketogenetic diet, often advocated for treatment of lactic acidosis, resulted in clinical deterioriation. Therapy with large doses of citrate, possibly acting as a TCA cycle substrate, resulted in clinical stabilization but continued poor development. These two patients appear to represent a new variation of congenital lactic acidosis which have not responded to conventional forms of therapy.

873 URINARY ACIDIC GLYCOHYDROLASE AS AN INDEX OF EARLY RENAL DAMAGE IN JUVENILE DIABETES MELLITUS (JDM). Elaine Kohler, Kumudchandra J. Sheth, and Thomas A. Good*, Medical College of Wisconsin, Milwaukee Children's Hospital, Department of Pediatrics, Milwaukee, Wisconsin.

Acidic glycohydrolases involved in the degradation of glycoprotein are present in small amounts in normal urines, but increase 4-fold in active renal diseases in children. To assess early renal involvement in JDM, Addis counts (timed urinary cell excretions), quantitative proteinuria, creatinine clearance, urinary acidic glycohydrolases, B-galactosidase (B-galase), B-N-hexosaminidase (B-hexase), and plasma acidic glycohydrolases, α-galactosidase, B-galase, B-hexase, α-mannosidase (α-mannase), α-fucosidase, were studied in 110 JDM children aged 3-16 years. Urinary B-galase and B-hexase was significantly higher in JDM than in normals, but lower than in children with active renal disease. Urinary B-galase, B-hexase had no correlation to urinary RBC's, WBC's, protein and sugar, but significantly correlated to plasma triglycerides, age of the child, and duration of JDM ($p<0.01$). Of the plasma glycohydrolase, B-hexase and α-mannase correlated to blood sugar, cholesterol, triglycerides and to age of the child and duration of JDM ($p<0.01$). Six hours after insulin, mean urinary B-galase and B-hexase in 18 children returned to near normal levels. These data suggest that both urinary and plasma acidic glycohydrolases may be used as an index of glycoprotein catabolism and hence early renal involvement in JDM.

874 ALTERED KINETIC PROPERTIES OF PYRUVATE DECARBOXYLASE IN A PATIENT WITH LACTIC ACIDEMIA. Yasuhiro Kuroda, Lawrence Sweetman, William L. Nyhan, Jeffrey Kline and Ted Groshong. University of California, San Diego, Dept. of Pediatrics, La Jolla, CA and University of Missouri, Dept. of Child Health, Columbia, MO.

Activities of the active and inactive forms of pyruvate decarboxylase (PDC) were measured in fibroblasts from normal individuals and a patient with congenital lactic acidemia, utilizing 10mM $MgCl_2$ to activate the enzyme from sonicated fibroblasts. The activities of the active and inactive forms in the patient were 0.56 ± 0.21 and 0.87 ± 0.33 and in the controls 8.01 ± 2.80 and 1.81 ± 0.39 nmoles/mg protein/hr. In the patient, the active form accounted for 39% of total PDC activity, while in the normals 77% of total PDC activity was present as the active form. The optimum pH (6.0) and Michaelis constants (Km) for pyruvate were similar in fibroblasts of the patient and controls. PDC activity was more sensitive to denaturation by heat in the fibroblasts of the patient than those from controls. Incubation for 5 minutes at 46.5°C led to a complete loss of activity in the patient, while there was still 25% of original activity in the controls. This difference in heat stability may be related to the difference in the ratio of active to inactive forms between the fibroblasts from controls and the patient. It suggests an altered molecular form of the enzyme protein as a result of a mutation in a structural gene.

875 EFFECT OF DIPHENYLHYDANTOIN(DPH)ON ARGININE-INDUCED GLUCAGON(IRG) SECRETION IN JUVENILE DIABETES MELLITUS (JDM). Vinod R. Lala, Christina S. Juan,Theodore W. AvRuskin. New York Univ.Sch.Med., The Brookdale Hosp. Med. Ctr., Dept. of Ped.,N.Y.,N.Y.

DPH has blocked IRG secretion in vitro(JCEM 35: 823,1972)To evaluate DPH effects on α cell function in JDM, 9 controlled pts. (5♀,4♂), ages 12-17 yrs.,were studied with paired Arginine infusion tests (AIT) after 12-hr. fasts, and 3 days of isocaloric diets. Following AIT-1,DPH(3mg/kg)was infused not to exceed 100 mg/min.After 20 min.,AIT-2 was done.Serial blood samples for BS and IRG were obtained over 300 min. IRG was measured by RIA using 30 K antisera and dextran-charcoal separation,with 95% confidence limits of ±26 pg/ml.Mean pre-and post-DPH BS increments were 75±13 and 67±13 mg/dl.Mean fasting pre-and post-DPH IRG were 174±34(M±SE)and 186±37.Mean pre-and post-DPH ΔIRG were 273±79 and 212±49.Mean % decrement in ΔIRG after DPH was 14.2±11.0(NS). Five pts. had 40.4±3.8 mean % decrement in ΔIRG post DPH. Absolute ΔIRG pre-and post-DPH in this group were 352±130 and 213±77($P>0.05$). Three randomly selected patients on bidaily Insulin therapy received 6 mos.DPH (5mg/kg/day). Single AIT were done at 0,5, and 180 days.Mean fasting IRG values were 140±33,122±24,175±57; mean ΔIRG values were 159±41,175±48,and 161±28 pg/ml,respectively. There was no significant statistic correlation between duration of JDM,age of pt.,or insulin therapy and DPH effect on arginine-induced IRG secretion.This study appears to be the first in vivo evaluation of DPH effects on alpha-cell function in JDM suggesting some modification of arginine-induced IRG secretion.

876 UPTAKE OF GLUCOSE AND RELEASE OF GLUCONEOGENIC PRECURSORS BY THE HINDLIMB OF THE FASTING BABOON NEONATE. Lynne L. Levitsky, John B. Paton, David E. Fisher and Clarence W. De Lannoy. Pritzker Sch. Med., Univ. Chicago, Michael Reese Hosp. Med. Ctr., Dept. Peds., Chicago.

Uptake of glucose and release of gluconeogenic precursors by the hindlimb of the fasting baboon infant was evaluated in 6 baboon neonates after delivery by cesarean section at term and 8 6-week-old baboon infants. Arteriovenous (AV) differences across the hindlimb were determined by measuring substrate levels in the aorta and the inferior vena cava below the level of the renal veins and above a unilaterally occluded femoral vein.

Substrate mM/L		Glucose	Lactate	Alanine	Glycerol
Birth	Arterial	2.43±.11	2.73±.17	.307±.012	.302±.031
	AV	- .40±.05	1.00±.14	.037±.004	.059±.010
6 weeks	Arterial	2.91±.11	1.18±.07	.139±.017	.321±.063
	AV	- .21±.02	.59±.09	.041±.008	.111±.017

There were no significant AV differences for pyruvate, beta-hydroxybutyrate, glutamate or glutamine. Production and uptake was calculated using hindlimb blood flows determined by the radioactive microsphere method. Glucose consumption by the hindlimb in the neonate was 2.4 µM/min. Uptake by the entire carcass was estimated to be 9.6 µM/min, almost twice the previously estimated cerebral cortex glucose consumption (5.6 µM/min). Estimated splanchnic and renal glucose production (15.7 µM/min) could account for all (15.2 µM/min) of estimated cerebral and carcass glucose uptake. The fasting neonate has a substantial glucose utilization rate exclusive of the requirement of the central nervous system.