718 EFFECT OF METHYLENE BLUE ON FIBROBLASTS IN LACTIC ACIDOSIS. Paul R. Goodyer and Gerald Lancaster (Spons. by Charles R. Scriver). McGill University, Montreal Children's Hospital, MRC Genetics Group and Division of Pediatric Nephrology, Montreal, Canada.

A girl presented on the 9th day of life with familial lactic acidosis, euglycemia and hepatomegaly; death occurred at day 15. Ratios for plasma lactate: pyruvate (130:1) and B-hydroxybutyrate: acetoacetate (38:1) were elevated suggesting an imbalance of tissue NAD:NADH. Plasma pyruvate (0.25mM, Norm = <.07mM) and alanine (1.7mM, Norm = <.4mM) were both elevated indicating a defect in pyruvate utilization. Organic acids other than those above were not elevated in urine. Skin fibroblasts produced excess lactic acid in culture. Evolution of $^{14}CO_2$ (nmoles/mg prot · hr ± S.D.) from 1mM L-1^{14}C lactate (control = 19.8 ± 9.4), L-1^{14}C pyruvate (control = 41.1 ± 4.7) or L-U^{14}C alanine (control = 12.7 ± 4.1) was markedly decreased compared to control cells (< 10%, < 1% and <10% respectively). Thiamine (0.7mM) or lipoic acid (0.01mM) for 1 or 24 hours of preincubation had no effect. Dichloroacetate (50μM) produced a modest increase of lactate utilization (150% increase) in the patient's cells, but the effect of methylene blue on alanine utilization (0.27mM) was dramatic (1200% increase), bringing it within the normal range (7.8-20.5nmoles CO_2/mg prot · hr).

Our findings suggest that methylene blue can repair lactic acidosis in vitro and may be of use in patients whose cellular regeneration of NAD is impaired.

719 AN ALTERNATIVE INTERPRETATION OF THE ENZYME DEFICIENCY IN THE GUNN RAT. Glenn R. Gourley, William Mogilevsky, Gerard B. Odell. University of Wisconsin Medical School, Clinical Science Center, Dept. of Pediatrics, Madison WI.

Bilirubin glucuronyl transferase activity (BGT) is negligible in jaundiced (jj) Gunn rats, with intermediate and higher levels in heterozygous (Jj) and outbred (JJ) rats, respectively. This could be explained either by a defective enzyme or structural defects in the endoplasmic reticulum in which the enzyme is compartmented. If the latter interpretation is correct, similarly segregating activities might be expected among other microsomal enzymes. The activity of aminopyrine demethylase (AD), a hepatic microsomal mixed-function oxidase, was assayed in male jj, Jj, JJ Gunn and Wistar (Wi) rats. BGT (μg bilirubin conjugated/30 min/mg protein N) and AD (nmoles CH_2O produced/min/mg protein) are shown below (mean±SD). Results: jj AD < Jj, JJ or Wi AD ($p < .05$). F-test demonstrated AD variance in Jj > jj or JJ rats ($p < .05$). A correlation ($r=.81$) exists between BGT and AD ($p < .01$) in JJ rats, but not in Jj rats. The data suggests a microsomal membrane defect in enzyme compartmentation may be the primary abnormality in the Gunn rat and possibly in Crigler-Najjar Syndrome.

ENZYME	jj(n)	Jj*(n)	Jj§(n)	JJ§(n)	Wi(n)
BGT	--	28.3 (15) ±7.1	28.0 (13) ±5.2	66.7 (10) ±10.8	50.2 (9) ±9.4
AD	12.58 (12) ±2.02	14.75 (15) ±3.82	14.52 (13) ±3.09	15.61 (10) ±1.80	14.76 (9) ±3.50

*Non-jaundiced offspring of Jj x jj, or (§) Jj x Jj matings.

● **720** COMMUNICATION SKILLS AMONG UNSELECTED XXY BOYS. John M. Graham, Jr., Anthony S. Bashir, Stanley Walzer, Rachel E. Stark, Park S. Gerald, Dept. of Maternal and Child Health, Dartmouth Medical School, Hanover, New Hampshire, Children's Hospital Medical Center, Boston, Johns Hopkins Medical School, Baltimore, Univ. of Mass. Med. Center, Worcester.

Previous studies of XXY boys from biased sources of ascertainment have suggested a risk for communication disorders, and ongoing longitudinal prospective studies of unselected XXY boys have demonstrated early lags in speech development. This study compares the communication skills of a group of 14 unselected XXY boys ascertained during a neonatal screening survey with a group of 15 normal control boys, matched for age, grade, performance IQ, birth weight, parental age and education, parity and socioeconomic status. Although the XXY group did not significantly differ from the control group in performance IQ, they did demonstrate a significant reduction in verbal IQ ($p \leq 0.001$), which resulted in a reduced full scale IQ ($p \leq 0.01$). The reduction in verbal IQ was correlated with significant reductions in auditory processing abilities, auditory memory, and expressive language. Of particular interest was the demonstration of word-finding difficulties and problems in the use of syntax as major factors in the expressive language deficit. Except for difficulties with syntax, receptive language skills were relatively normal. These results suggest that left-hemisphere-based difficulty in serial order processing may be associated with the XXY anomaly, as compared with right-hemisphere deficits in spatial processing that have been associated with XO Turner syndrome.

721 EFFECT OF CHOLESTEROL IN PROPIONYL CoA CARBOXYLASE (PCC) DEFICIENCY. Robert E. Grier and Barry Wolf (Spon. H.M. Maurer). Medical College of Virginia, Departments of Human Genetics and Pediatrics, Richmond.

Propionate is formed by the catabolism of isoleucine, valine, threonine and methionine, by the oxidation of odd-numbered carbon chain fatty acids and by the degradation of the three-carbon side chain of cholesterol. Because propionate and its metabolites accumulate in the tissues of PCC-deficient patients, the therapeutic limitation of dietary branched-chain amino acid and fatty acid intake is recommended. However, the effect of dietary cholesterol on propionate metabolism in PCC-deficient patients has never been investigated adequately. A large oral dose of cholesterol was administered to each of two patients, a 10-yr. old previously symptomatic male and his 14-yr. old asymptomatic sister. Both children were metabolically stable on a 0.8 to 1.2g protein/ kg/day diet. After a control period, each child was administered 25 mg/kg of unconjugated cholesterol in a single dose. Their serum cholesterol levels increased 3-10%, whereas their serum electrolyte and glucose concentrations remained unchanged. Their serum propionate concentrations did not increase significantly, but the boy's serum ammonia concentration increased from 37 μg/dl (nl: 7-50 μg/dl) at 4 hrs to 105 μg/dl at 8 hrs after administration of the load with no change in his mental status. Although our results provide no clear indication that cholesterol is harmful in PCC-deficient patients, the elevation of ammonia in the symptomatic patient raises the possibility that dietary cholesterol intake should be monitored in PCC-deficient patients along with the other precursors of propionate.

722 AMYOPLASIA: A DISTINGUISHABLE FORM OF ARTHROGRYPOSIS Judith G. Hall, Susan D. Reed, Garry Greene, Ellen P. Driscoll. Departments of Medicine & Pediatrics, Children's Orthopedic Hospital and Medical Center and University of Washington School of Medicine, Seattle, Washington 98105

A specific type of arthrogryposis has been recognized among 135 (39%) patients in a study of over 350 patients with congenital contractures of the joints in 2 or more body areas. It was designated "amyoplasia" because the condition is characterized by absence of muscle tissue with fibrosis and fatty replacement. A characteristic positioning of the limbs is present at birth. Intelligence is normal and the condition appears to be sporadic with no known familial recurrence. Chances of survival are excellent but disability can be marked. Early mobilization with physical therapy is important. An excess (11/135) of discordant identical twins has been observed.

Typically, the shoulders are internally rotated with decreased muscle mass, the elbows are usually extended (70%) with flexion contractures of the wrists and hands. Severe equino varus deformities of the feet are seen in about 90% of the patients. Most affected patients have 4-limb involvement (85/135; 63%), but some have mainly upper limb involvement (17/135; 13%) and others have mainly lower limb involvement (33/135; 24%). The face is usually round with a midline hemangioma. In general, there are no associated visceral malformations; however, deformation anomalies are seen at a higher frequency than expected (amniotic bands, smashed digits, cord wrapping, skin tags, cryptorchidism, craniosynostosis, dislocated radial head, scoliosis, etc.). Pathological studies of muscle and spinal cord have been non-specific.

723 ANTENATAL DETECTION OF CYSTIC FIBROSIS. Catharine J. Harris, Kathi Mesirow, Phyllis Rembelski, Henry L. Nadler. Northwestern Univ. Med. Sch., Children's Memorial Hospital, Dept. of Pediatrics, Chicago, Illinois

Preliminary studies previously reported by our laboratory have suggested that quantitative and qualitative measurements of methylumbelliferylguanidinobenzoate (MUGB) reactive proteases in mid-trimester amniotic fluid may provide an approach to the antenatal detection of cystic fibrosis. During the past year, we have evaluated thirty additional amniotic fluids using a combination of quantitative measurements of MUGB, isoelectric-focusing, and gel filtration, bringing the total number of high risk pregnancies monitored to forty-three. Eighteen pregnancies have come to term, fifteen from obligate heterozygote parents. Sweat chloride analysis has confirmed our prediction of fifteen normal and three affected with cystic fibrosis. Three additional pregnancies, predicted to be affected, were electively terminated. Unfortunately, confirmation is not possible. There has been one spontaneous abortion and one stillbirth. The stillbirth, predicted in 1979 to be normal by only two tests, had evidence of meconium peritonitis on autopsy. This case, therefore, may represent a missed diagnosis. The remaining twenty pregnancies will come to term within the next five months. These data suggest that this approach may provide a clinically useful means for antenatal detection of cystic fibrosis.