350 ABNORMAL NOCTURNAL GROWTH HORMONE (GH) SECRETION IN SHORT CHILDREN WITH CRANIOFACIAL MALFORMATIONS SYNDROMES (CMS). Yolaine St. Louis, Richard HK Wu, Michael J. Thorpy, Robert Shprintzen, Scott Breidbart, Edna H. Sobel and Paul Saenger. Albert Einstein Coll. Med., Montefiore Hosp.&Med. Ctr., Depts. Peds.,Sleep-Wake and Craniofacial Ctrs., Bronx, New York.

Children with CMS (Treacher-Collins Syndrome, hemifacial microsomia, Robin Sequence, Stickler Syndrome and other syndromes of clefting) and obstructive airway disease have poor sleep-entrained growth hormone (GH) secretion and may grow poorly. We studied GH release in four patients with CMS and compared it to seven children with idiopathic short stature (ISS) by measuring GH in blood, every 20 min. during sleep. All patients had GH concentrations $\geq$ 10 ng/ml during standard provocative testing and had subnormal (<2 SD) height and height velocity percentiles for age. No patient had significant apnea or oxygen desaturation during the sleep period. GH secretory rates/per hour of sleep obtained by calculating area under the curve divided by sleep time (hrs) for CMS vs ISS were 8.4±4.0 vs 20.8±9.4µg/hr (mean ± SD) ($p<0.025$). There was no difference in the mean amplitude of the highest GH peak obtained during sleep: 13.4±4.7 ng/ml vs 19.2±6.6 ng/ml for ICM vs ISS ($p>0.05$). CMS patients had histories of poor sleep at home but no apnea was demonstrated during overnight studies. These data suggest that children with CMS who grow poorly may have insufficient GH secretion during sleep.
Conclusions: Children with CMS and short stature require nocturnal GH secretion studies as part of their evaluation because nighttime GH secretion may be deficient and they may therefore benefit from treatment with growth hormone.

351 AN AFFECTED FEMALE CARRIER OF DUCHENNE MUSCULAR DYSTROPHY WITH ASSOCIATED MITRAL VALVE PROLAPSE J.Towbin, E. R. B. McCabe, J. F. Hejtmancik, D.G. McNamara, C. T. Caskey, Baylor College of Medicine, Institute for Molecular Genetics and Section of Pediatric Cardiology, Houston.

Mitral valve prolapse (MVP), cardiomyopathy (CM), and conduction disturbances have been associated with Duchenne muscular dystrophy (DMD). This X-linked disorder characteristically manifests symptoms in males in the first five years of life due to pelvic girdle muscle involvement. Rapid progression to other skeletal muscles occurs before cardiac involvement. Classically females are considered asymptomatic carriers diagnosed by elevated serum enzymes. Recently Kunkel et al demonstrated a large gene locus for DMD in the Xp21 region, but specific myocardial coding regions have not been elucidated. MVP syndrome in DMD has been proposed to be an expression of underlying CM and papillary muscle dysfunction. Speculation of occurrence in asymptomatic carriers has been made. We present a 20 year old affected female carrier with strong family history for DMD and complaints of progressive leg weakness and new onset cardiac murmur. Leg weakness, positive Gowers' sign, midsystolic click and apical late systolic murmur were clinically noted, in addition to extremely elevated serum CPK (5263mU). Echocardiography (M-mode, 2-D, Doppler) demonstrated mitral regurgitation and normal shortening fraction. DNA diagnostic studies using multiple probes showed maternal 754, pERT, and XJ1.1 alleles (similar to carrier sister). We conclude that MVP syndrome in DMD does occur in female carriers and improved molecular diagnostic testing aids the clinical assessment.

●352 MYOPATHY (SKELETAL AND CARDIAC) AND WHISTLING-FACE SYNDROME (WF). Wladimir Wertelecki, David G. Laycock, and Duane W. Superneau, University of South Alabama College of Medicine, University of South Alabama Medical Center, Department of Medical Genetics, Mobile.

Diagnosis of the Whistling-Face syndrome (WF) usually follows the observation of microstomia and a stigmatic facies associated with ulnar deviation of fingers and joint contractures. Muscle atrophy and myopathy, although reported in WF, receive insufficient emphasis. More recently, cardiomyopathy and malignant hyperthermia have been observed in WF patients. Our clinical studies and review bring support to the conclusion that the spectrum of WF includes: skeletal weakness, hypertrophic cardiomegaly with WPW conduction abnormalities (unresponsive to quinidine), and elevated serum CPK, GOT, and LDH. Hypertrophic cardiomyopathy with enlarged myofilaments due to abundant amyloid-like material, and skeletal myopathy with scattered fiber atrophy and focal areas of fatty deposition and myelin fibers, are also part of WF.

Consequently, individuals with primary hypertrophic cardiomyopathy or a history of malignant hyperthermia should also be assessed for clinical features of WF and vice versa. Because WF presents with clinical variability and is an autosomal dominant disorder of prenatal onset, a family history of any of the features described above may be pertinent in genetic counseling and prenatal assessment of families with WF syndrome.

353 LANGUAGE AND DEVELOPMENT IN THE "FG" SYNDROME. Bruce E. Wilson, Peggy McCardle, and Sondra Warren Levin. (Spon. by Itzhak Brook) Walter Reed Army Med Ctr, Dept of Peds, Washington, DC; and USUHS, Dept of Peds, Bethesda, MD.

The "FG" Syndrome is an X-linked syndrome characterized by unusual facial features, cardiac defects, mental retardation and gastrointestinal anomalies. Agenesis of the corpus callosum has also been noted in this syndrome. We report sequential language and developmental testing in a patient with "FG" syndrome, including callosal agenesis. J.B. is a 4 year 6 month old white male who has shown progressive delay in language and development. When first tested at 25 months of age, he had a 7 month receptive delay and an 11 month expressive delay. By 34 months of age, both were delayed by 14 months. At 54 months, his receptive skills were 21 months delayed and expressive skills were 24 months delayed and neither had shown measurable progression over the preceeding 10 months. He has abnormal articulation, word finding difficulty, and disordered syntax. This pattern of speech development is consistent with the language function defects reported in adults with callosal agenesis. His motor skills have been similarly delayed, and he has been consistently unable to anticipate his own manual adjustments. His skills on the Bayley and selected McCarthy subtests place him in the mildly mentally retarded range. Some of the deficits noted are consistent with a defect in interhemispheric communication. This pattern of progressive developmental and language delay has not been previously reported in the "FG" syndrome.

●354 A NEW X-LINKED RECESSIVE SYNDROME WITH BRAIN, HEART AND GENITAL MALFORMATIONS Vickie L. Zurcher, Ali M. Yazdy, (Spons. by Irwin A. Schafer), Case Western Reserve University at Cleveland Metropolitan General Hospital, Department of Pediatrics, Cleveland, Ohio.

The proband, a 2.9 kg term male, was live-born and died on day 5 of life following cardiopulmonary arrest. Autopsy revealed aqueductal stenosis with hydrocephalus; agenesis of the septum pellucidum, olfactory bulbs and tracts; focal cerebellar dysplasia; cystic lesions of the ganglionic eminence; acute and remote cerebral infarcts; aortic coarctation with a dysplastic, bicuspid aortic valve; ASD; VSD; severe hypospadias; sacrococcygeal sinus; left foot equinovarus deformity; simple low set ears; fifth finger clinodactyly; and abnormal palmar creases. The proband's half brother through a common mother was a pre-term infant who expired at age 13 days. Autopsy revealed aqueductal stenosis with hydrocephalus; cerebral and cerebellar dysplasia with neuronal and glial heterotropias; intraventricular hemorrhage; aortic dextroposition; pulmonary valve atresia; VSD; PDA; severe hypospadias; thoracic spina bifida occulta; low set ears; and unusual finger overlap. Both infants were 46,XY. Their mother had a maternal uncle with a large head and abnormal genitals who was stillborn, and a maternal aunt delivered a hydrocephalic stillborn male. Autopsy records are unavailable on these latter individuals. There have probably been four affected males in three generations of this family. This syndrome, which is of unknown embryologic pathogenesis, appears to be inherited as an X-linked recessive disorder.

DEVELOPMENTAL PHARMACOLOGY

355 VITAMIN E PHARMACOKINETICS: COMPARISON OF 1 VERSUS 8 HOUR INFUSION. Soraya Abbasi, Bradford K. Jensen, Lois Johnson, Christine Dalin. Univ. of Pennsylvania Sch of Med, Pennsylvania Hosp, Newborn Pediatrics, Phila, PA and Hoffmann LaRoche Inc, Nutley, NJ.

Premature infants are vitamin E deficient at birth. Vitamin E administration by infusion is preferable to intramuscular injection because of the small muscle mass of very low birthweight infants and the irritating nature of free tocopherol. Pharmacokinetics of intravenous vitamin E (IV) was evaluated in 9 preterm infants. 4 infants (Group 1, BW 990 ± 84 gms, GA = 29.2 ± 1.1 wks) were given a single dose of 10 mg/kg of dl-α tocopherol (Hoffmann LaRoche) by 1 hour infusion. The same dose was given to 5 infants (Group 2, BW 1138 ± 133.6 gms, GA = 28.4 ± 1.3 wks) by 8 hour infusion. Blood samples were obtained from central line immediately prior to (zero time) and at 2,4,6,8,10,12,15,18,24,36,48,72 hours after vitamin E infusion. Pharmacokinetic parameters were obtained by model independent analysis of the serum vitamin E concentration time profile. Mean ± SD values for harmonic half life (T 1/2, hrs), volume of distribution (VD, liter/kg), serum clearance (SC ml/hr/kg) and selected serum vitamin E levels (E, mg/dl) for the two groups are:

	T 1/2	VD	SC	0 time	Peak	24 hrs
Gr 1	69.3	0.39 ±.17	3.4 ± 1.7	.6 ±.3	16.3 ± 5	3.4 ± 1.5
Gr2	69.3	0.31 ±.09	2.8 ± 0.9	.5 ±.1	4.7 ± 1	2.3 ± .8

Infusion of vitamin E over 1 hour results in a significantly higher peak but similar steady state values as compared to 8 hours. These data can be used for dosing recommendation.