919 TRISOMY 5p: A VARIABLE PHENOTYPE. J. F. Cordero, W.A. Miller, R.M. Liberfarb, L. Atkins and L.B. Holmes. Mass. General Hospital, Boston, MA.

The availability of differential staining techniques has led to the identification of many new chromosome abnormalities. We have recently evaluated three unrelated families in which five children have been handicapped to varying degrees as a result of a duplication of the short arm of chromosome 5.

In each of two families, one parent had a balanced chromosome translocation which was the basis for the chromosome imbalance in four children. Another infant was the first affected family member.

In Family G. there are two retarded females with no malformations and a partial 5p trisomy; i.e., 46,XX,der(8),t(5;8)(p13;p23) mat. In Family T. a brother and sister had multiple congenital anomalies. The karyotype in the girl showed 46,XX, der(9),t(5;9)(p13;p24) pat. In Family E. a male infant with hypotonia and club feet had a chromosome complement of 47,XY, $5p^-$,+i(5p) e.g. centric fission of chromosome 5 with duplication of the short arm.

These five children are all mentally retarded, but their associated physical findings vary from no abnormalities to multiple malformations. Possible explanations for this phenotypic discrepancy include varying degrees of duplication of chromosome 5 and the presence of an associated chromosome deletion in the unbalanced translocation. The child with the isochromosome 5p may be more indicative of the 5p trisomy syndrome.

920 A FAMILIAL THYRO-CEREBRAL-RENAL SYNDROME: A NEWLY RECognized disorder. Edward A. Cutler, Jack Bass, Carolyn A. Romshe, Ala B. Hamoudi, David Bachman, Stella B. Kontras, Juan F. Sotos. College of Medicine, The Ohio State University and The Children's Hospital Research Foundation, Department of Pediatrics, Columbus, Ohio 43205.

A brother and sister had renal, neurological and thyroid disease; both with normal mentality. The sister presented at one year of age with evidence of renal disease (BUN 35 mg/dl). At age 9 neurological deterioration, muscle wasting, ataxia and myoclonus developed. Diffuse goiter was present (T_4 RIA 5.0 µg/dl; thyroid microsomal antibodies 1:100; I^{131} uptake 8% at 2 hours. Perchlorate discharge was 50%, indicating a possible organification defect). Sensorineural deafness was demonstrated. Platelets were low (20,000) and serum zinc was high (570 µg/dl). Hyperuricemia persisted (10.3 mg/dl). The condition progressed with generalized muscular weakness, hemiparesis, clonic-tonic seizures and increasing renal insufficiency. BUN was 120 mg/dl and serum creatinine 1.5 mg/dl. The discrepancy between BUN and creatinine persisted. Kidney biopsy and post-mortem examination showed interstitial and tubular nephropathy with secondary glomerular sclerosis with negative immunofluorescence, simple colloid goiter and degenerative and focal demyelination of the cerebral white matter and extensive neuronal loss and demyelination of the cerebellum.

The brother is 13 years old and has interstitial nephritis (two biopsies), slurred speech, headaches, thrombocytopenia, an abnormal EEG and goiter.

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921 BIOCHEMICAL AND GENETIC BASIS OF PALATAL SHELF FUSION IN MICE: H-2, cAMP-MEDIATED VERSUS H-2, CORTICOSTEROID MEDIATED EFFECTS. R. P. Erickson & M. S. Butley. University of Michigan Medical School, Departments of Human Genetics and Pediatrics, Ann Arbor 48109.

On a biochemical level, both steroids and cAMP are known to play a role in palate formation. cAMP levels rise prior to fusion, inducing epithelial cell death and adhesiveness. Steroid injections increase the incidence of palatal clefting; the magnitude of the effect is strain dependent, and strains which are less susceptible have been shown to have fewer steroid receptors. On a genetic level, susceptibility to steroid-induced cleft palate is H-2 linked. Basal cAMP levels in some tissues also appear to be H-2 determined. The mechanism by which steroids induce cleft palate is unknown, but cAMP may be involved. Premature cell death and/or glycocalyx formation as a result of abnormally high levels of cAMP might well prevent subsequent growth and fusion of shelves. H-2 might mediate its effect through control of basal or steroid-induced cAMP levels, through both, or neither. To determine the relationship between steroids, cAMP, palatal fusion, and H-2, we have been measuring the developmental curve of palatal shelf cAMP levels in congenic lines differing in both H-2 and cleft palate susceptibility, with and without steroid injections. To date, no difference in basal palatal shelf cAMP levels have been found. Steroid induced levels are significantly higher, but strain differences are not yet apparent. The results do not indicate whether steroids are exerting a permissive effect on cAMP levels or whether the more usual, transcriptional control mechanism is at work.

922 TRICHO-RHINO-PHALANGEAL (TRP) SYNDROME: VARYING EXPRESSIVITY AND PROGRESSION OF SKELETAL ABNORMALITIES. J. L. Frias, A. H. Felman, A. D. Garnica and S. E. Wallace (Spon. by O. M. Rennert), Univ. Florida College of Medicine, Dept. Pediatrics and Radiology, Gainesville.

TRP syndrome includes pear-shaped nose; thin, slowly-growing hair and clinobrachydactyly with cone-shaped epiphyses. Most reports have dealt either with few affected individuals within a family or with sporadic cases, thus limiting the recognition of the scope of manifestations of the syndrome and the definition of its mode of determination. This records the first pedigree involving multiple affected members in three generations. Fifty percent of individuals born to an affected parent had TRP syndrome, sex ratio was 1:1 and there was male to male transmission, confirming autosomal dominant inheritance. Evaluation of 21 affected individuals (ages newborn to 65 years) demonstrated variability in expression with most of the characteristic features present in 18 and lack of hair changes or facial abnormalities with minimal hand involvement and normal stature in the rest. Pattern profile of the hands helped corroborate the diagnosis in mildly affected patients. Older individuals showed progressive kyphoscoliosis, pectus carinatum and protrusio acetabulae. Epiphyseal changes other than coning, such as small size, fragmentation and aseptic necrosis, were observed in several individuals. A 34-year-old patient with aseptic necrosis of the femoral heads required bilateral hip prosthesis. Our observations emphasize the need to periodically evaluate the extent of skeletal involvement in affected individuals and to examine parents of presumably sporadic cases to detect minimal expressivity.

923 DELETION OF THE LONG ARM OF CHROMOSOME #4. A CLINICALLY IDENTIFIABLE SYNDROME? Jaime L. Frias, Robert M. Nelson and Shari L. Ray (Spon. by Owen M. Rennert), University of Florida College of Medicine, Department of Pediatrics, Gainesville.

A deletion of the long arm of chromosome #4 [46,XX,del(4)(q31)] was demonstrated in a 3-month-old male with multiple congenital malformations and marked psychomotor retardation. The child, delivered by C-section at 38 weeks gestation, weighed 2,600 gm. Hypotonia and cyanosis upon crying or feeding, without demonstrable congenital heart disease, were evident from birth. Postnatal growth and development were retarded. Malformations included a small head with prominent occiput and asymmetric forehead; narrow facies; posteriorly rotated and poorly developed ears; dysplasia of the inner canthi and mongoloid slant to the palpebral fissures; cleft lip, cleft palate and micrognathia; congenital hip dysplasia; abnormal implantation of the thumbs and toes and bilateral simian creases.

Three other infants with a deletion of the long arm of #4 have been reported in the literature. Although the study of additional cases will be necessary to more completely define the phenotype, the similarity of the pattern of malformation found in our patient and in those previously reported in the literature suggests that the 4q- syndrome may constitute a clinically identifiable disorder.

924 LEFT-SIDED HEMIFACIAL MICROSOMIA AND TETRALOGY OF FALLOT. J.M. Friedman and Alexander J. Muster (Spon. by Henry L. Nadler) Northwestern University Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois

Six patients with significant congenital heart disease were found to have hemifacial microsomia. Five of the patients, all of whom are males, have Tetralogy of Fallot. The sixth has a closely related cardiac malformation: double outlet right ventricle. Unlike most individuals with oculoauriculovertebral dysplasia, all of these patients have developmental retardation and 5 of the 6 have predominantly left-sided facial involvement. The sixth child has right facial hypoplasia but a left preauricular tag. None of the patients has the characteristic ocular abnormalities of the Goldenhar syndrome, but in all 6 additional malformations were observed. These included vertebral anomalies (4), abnormal ribs (2), renal malformations (2), cleft soft palate (1), occipital dural sinus (1), and hypoplastic first metacarpal (1). It is suggested that Tetralogy of Fallot and related congenital cardiac malformations may be especially common among male patients with oculoauriculovertebral dysplasia who have left-sided hemifacial microsomia.