

**338** CONGENITAL COMPLEX CHROMOSOME REARRANGEMENTS (CCR). Boris G. Kousseff, Yau-Ping Essig, Richard L. Neu. Univ. of South Florida, Dept. of Ped., Tampa. Congenital CCR have been reported in over 50 patients divided into a familial and de novo categories. Between 1982 and 1986 we saw three unrelated children with de novo (parents had normal karyotypes) unbalanced congenital CCR. Lymphocyte and fibroblast karyotypes were studied using G, Q, C, R and NOR banding.

Patient 1. A premature (33 weeks) newborn female (BWT 2 kg, HT 38 cm, OFC 30 cm) had cleft lip and palate, telecanthus, choanal atresia and ectrodactyly of hands and feet. The karyotype showed  $t(2;5)(q33;q22)$ ,  $t(3;11)(q27;p11.2)$  and  $del(13)(q12q14)$ . The five derivative chromosomes implied six breaks.

Patient 2. A 3 months old female (BWT 2.3 kg, HT 42.5 cm, OFC 31 cm) product of a term pregnancy with oligohydramnios and normal placenta, had cleft lip and palate and mild facial dysmorphism. Subsequently microcephaly and slow growth were noted. The karyotype showed six derivative chromosomes:  $t(2;3)(q33.2;p22.5)$ ,  $t(7;18)(q32;q12.2)$ , two  $inv(2)$ ,  $(p12q24)$  and  $(q31q33)$  and  $del(10)(p13)$  implying nine breaks.

Patient 3. A 12 year old male with IQ of 40, HT < 3rd % tile, scoliosis and mild dysmorphism had BWT 3 kg, HT 48.5 cm and unremarkable neonatal period. His karyotype showed seven derivative chromosomes:  $t(2;11)(q21;p14)$ ,  $t(5;15)(p11;q11)$ ,  $t(6;11)(p23;p14)$ ,  $t(6;20)(p23;p13)$ ,  $del(6)(q26)$  and  $del(14)(q24)$  implying eight breaks.

The phenomenon of congenital CCR in man appears real and the pediatrician should know about it.

**339** COCKAYNE SYNDROME (CS) MASQUERADING AS SECKEL SYNDROME (SS). James M. Lewis, (Spon. by Ruth C. Harris). Marshall University School of Medicine, Department of Pediatrics, Huntington, WV.

Our patient presented at 3 months of age with microcephaly, nystagmus, optic atrophy and developmental delay. Birth weight was 2.7 kg. At 11 months he was labeled as SS on the basis of microcephaly, short stature and facial features. Over the next 4 years he developed marked growth failure, mental retardation, ataxia, sunken eyes, photosensitivity, and dental caries. Kyphosis, contractures, lens opacities and long extremities with shortened trunk were present at the time of death at 8 years of age. We identified 132 CS case reports in the world literature comprised of 72 males and 56 females (4 undescribed). Mean ( $\pm$ S.D.) birth weight was 2.9(0.6)kg. Mean age at death (27 cases) was 14(+8) years. The most common neurologic abnormalities noted were mental retardation (90%), microcephaly (83%), motor disturbance (71%), deafness (47%), intracranial calcification (39%), ventricular dilatation (23%) and peripheral neuropathy (21%). Reported physical manifestations were cachectic dwarfism (91%), characteristic facies (89%), photosensitivity (60%), contractures (52%), long extremities with shortened trunk (43%), dental caries (42%), small or undescended testes (38% of males), kyphosis (21%). Ophthalmologic features included retinal pigmentation (51%), optic atrophy (37%), and cataracts or lens opacities (27%). CS is an autosomal recessive leukodystrophy with considerable variation in the expression and progression of clinical manifestations. The constellation of clinical features and the inexorable course of physical and mental deterioration which distinguish CS from SS will be discussed.

**340** RETT SYNDROME: ADDITIONAL FINDINGS FROM 7 CASES John B. Moeschler, Catherine E. Charman, Susan Z. Berg, John M. Graham, Jr., (Spon. by R.Z. Klein). Dartmouth Medical School, Dartmouth-Hitchcock Medical Center, Clinical Genetics and Child Development Ctr. Dept. of Maternal & Child Health, Hanover NH 03756

This paper summarizes the clinical findings of 7 girls diagnosed in 1985-86 as having Rett syndrome. Ages ranged from 3.5 to 25 years. Abnormalities of gestation were noted: Neonatal feeding problems (3/7) and positional deformities (3/7) [including hip supplantation (1), metatarsus adduction (1), "windswept feet" (1)] were identified. Postnatal growth abnormalities included: 7/7 head growth deceleration, 3/7 microcephalic, 7/7 statural growth deceleration, 6/7 short stature. In 6/7 girls, developmental delays were noted prior to true psychomotor regression. In only one girl was there clear documentation of normal development followed by marked deterioration. Age at onset of delays ranged from 6-12 months, with psychomotor regression noted from 10-34 months. Typical hand stereotypy started between 2-3 years in all. Other findings: 6/7 trunk ataxia, 1/7 ambulatory (with gait apraxia), 6/7 seizures, 5/7 strabismus, 4/7 scoliosis, 6/7 had irritability and/or self-injury with music or motion helpful in 2 girls. These gestational abnormalities, neonatal findings and early psychomotor delays prior to regression are important additional phenotypic findings. Until a reliable genetic or biochemical marker is available, the diagnosis of this syndrome rests on the recognizable neurodevelopmental phenotype.

**341** PROXIMAL 15q DELETION IN A FATHER AND SON WITH ISOLATED OBESITY Jane E. O'Brien, Murray Feingold, Wayne A. Miller. The Prader-Willi Syndrome (PWS) has been described clinically as: obesity, hypotonia, acromicria, and mental retardation. The eating disorder is currently thought to have a hypothalamic basis. Recent reports have associated PWS with a deletion between bands q11 and q13 on chromosome 15. Studies of PWS patients with interstitial deletion frequently show the origin of the deleted chromosome to be paternal, although parental chromosomes have been normal. We are reporting an 8 year old boy with isolated obesity and the karyotype:  $mos46XY, 46XYdel(15)(q11.1q11.2)$ . History revealed normal developmental milestones. Height was 90%ile, weight >95%ile, and head circumference 90%ile. No dysmorphic features were noted. Hand length was at the 75%ile. He had normal tone and normal genitalia. The patient's father reported obesity in adolescence with a maximum weight of 102kg (>95%ile); height was 170cm (10%ile). His obesity resolved with strict dietary management starting at 22 years of age. He has normal intelligence, no dysmorphic features, and is the father of two children. His karyotype:  $mos46XY, 46XYdel(15)(q11.1q11.2)$ . Both father and son had approximately 60% normal cells and 40% deleted cells (lymphocyte culture). Neither father nor son has features of PWS other than obesity. We raise the possibility that the hypothalamic control of obesity is mediated at the q11.1-q11.2 region of the 15 chromosome. This deletion can be associated with isolated obesity as well as PWS.

**342** EFFECTS OF VITAMIN SUPPLEMENTATION ON THE OCCURRENCE OF NEURAL TUBE DEFECTS IN THE RAT. Janine E. Polifka, Heidi R. Russ and Robert L. Brent. Thomas Jefferson University, Department of Pediatrics, Phila., PA

Clinical studies have indicated that the incidence of neural tube defects (NTD) is lower in a population of women given supplemental vitamin therapy than in the control population of women (both groups having previously delivered an infant with a NTD). To further investigate the possible protective effects of vitamin supplementation during gestation, pregnant rats were initially injected, subcutaneously, with MVI-12, a multi-vitamin preparation or the vehicle preparation on the morning of the 8th day of gestation. One hour later, the rats were anesthetized and a laparotomy performed to confirm the number of embryonic sites. At this time, sheep anti-rat yolk sac serum (100 mg/kg) was administered intraperitoneally. This dose produces a 100% incidence of congenital malformations, including NTD. The incision was closed and the pregnancy allowed to continue to term. Vitamins continued to be administered over a period of three days to maintain high levels of vitamins in the rats. NTD were observed in 100% of the term offspring in both the vitamin-supplemented group and the control group. In addition, no reduction in embryoletality was found in the vitamin-supplemented group. These results suggest that vitamin supplementation, at least at the doses used, does not afford protection against the teratogenic effects of yolk-sac antisera in rat embryos. It has been hypothesized that NTD have multiple etiologies and, therefore, no single treatment will be likely to prevent these defects. These results do not refute that hypothesis. (Supported by NIH)

**343** AMYOPLASIA: AUTOSOMAL RECESSIVE INHERITANCE IN TWO FAMILIES. Daniel H. Polk, Robin D. Clark, Donna Eteson (Spon. by Larry Shapiro). Dept. of Pediatrics, King-Drew and Harbor-UCLA Medical Centers, Los Angeles and Torrance, CA.

Amyoplasia has been previously described as a sporadic congenital form of skeletal muscle dysplasia resulting in arthrogryposis. We presently follow two families in which amyoplasia is not sporadic but is probably inherited as an autosomal recessive trait. In the first family, a 31 year old gravida 5 parity 4 Hispanic mother delivered a female child via cesarean delivery at term. Salient features included arthrogryposis, decreased muscle bulk, decreased movements, bilaterally dislocated hips, moderate hirsutism, nevus flammeus of the forehead and a high arched palate. No central or peripheral nervous system abnormalities were demonstrable and muscle biopsy confirmed the diagnosis of amyoplasia. Family history revealed that the parents were first cousins and a sibling of the current patient died at four months of age with similar features. The sibling also failed to demonstrate any central or peripheral nervous system abnormalities and, on review, had a muscle biopsy consistent with the diagnosis of amyoplasia. The second family was referred for counseling after a four year old daughter with decreased muscle mass, arthrogryposis, minimal spontaneous movements, small mouth, long tapered fingers and toes and a nevus flammeus of the forehead was diagnosed as having amyoplasia. Family history revealed that the Hispanic parents were first cousins, once removed. Conclusion: Amyoplasia is a syndrome of heterogeneous etiologies and, in selected populations, may be inherited as an autosomal recessive trait.