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Concordance among monozygotic and dizygotic twins from a population-based sample for self-reported atopic triad, syndrome x, and psychiatric conditions. W.Y. Huang[1], W. Maier[1], L. Murrelle[2], L.A. Corey[2], L.J. Eaves[2], and N.S. Shepherd[1]. [1]Glaxo Wellcome Inc., RTP, NC and [2]Virginia Commonwealth University, Richmond, VA.

A population-based sample of 806 monozygotic (MZ) twin pairs and 553 dizygotic (DZ) twin pairs in the Mid-Atlantic Twin Registry has been analyzed. Since MZ twins are genetically identical (assuming no somatic mutations occur) and DZ twins, like non-twin siblings, share an average of half of their genes, the comparison of disease concordance between MZ and DZ twins can be used to test the degree of genetic involvement in the development of a particular trait. We observed a greater proband concordance rate among MZ twins relative to DZ twins for a number of diseases ([difference (95% confidence interval)] for self-reported asthma [0.33 (0.22-0.44)], hay fever [0.20 (0.14-0.26)], eczema [0.13 (0.04-0.22)], diabetes [0.18 (0.01-0.35)], hypertension [0.13 (0.04-0.22)], obesity [0.10 (0.0-0.20)], depression [0.30 (0.21-0.39)], and anxiety [0.16 (0.06-0.26)]). The concordance rates among twin/non-twin sibling pairs were similar to those among DZ twins across all the diseases under investigation ([differences (95% confidence intervals] ranging from [0.01 (-0.07-0.09)] to [0.09 (0.0-0.18)]) in 410 families with data available for both twin members and at least one of the non-twin siblings. The atopic triad (asthma, hay fever, eczema), and anxiety and depression had study population prevalence rates similar to the proband concordance rates in DZ twins; whereas all the syndrome X diseases (diabetes, hypertension, obesity) had higher proband concordance rates among DZ twins relative to their study population prevalences. The present study demonstrates the utility of self-report data in a large population-based sample and is the first to simultaneously study the genetic influences on multiple disease clusters using a twin registry. It confirms previous findings from single disease studies of a significant genetic influence on the risk of each disease in question, and supports the hypothesis that common genetic mechanisms may underlie each disease cluster.

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Oculoauriculofrontonasal syndrome in a nine-month-old male. H.A. Ishmael, M.L. Begleiter and M.G. Butler. Section of Medical Genetics and Molecular Medicine, The Children's Mercy Hospitals and Clinics, Kansas City, MO.

Oculoauriculofrontonasal syndrome (OAFNS) was initially described in 1983. Since that time there have been 18 patients reported in the literature with this rare presumed autosomal recessive syndrome. Individuals with OAFNS have clinical features in common with both the oculoauriculovertebral spectrum and the frontonasal dysplasia sequence. We present a nine month old Caucasian male with OAFNS. The patient was delivered at 38 weeks gestation to a healthy 39-year-old (G3P3) mother. The patient's parents were non-consanguineous and his two older brothers were unaffected. The remainder of the family history was non-contributory. A chorionic villus sampling was performed due to advanced maternal age and a normal 46,XY male karyotype was found. A cleft lip and a possible cerebral mass were identified by routine prenatal ultrasound. At birth, the patient was small for gestational age and had multiple congenital anomalies including bilateral cleft lip and palate, left pre-auricular skin tag, severely hypoplastic right pinna without an external canal, severely everted and hypoplastic left upper eyelid, notched broad nasal tip, ocular hypertelorism, and micrognathia. Further evaluations showed an extra cervical rib on the left, hemivertebrae at T3-4, agenesis of the posterior corpus callosum with a midline lipoma, an extra renal pelvis on the left, a small patent foramen ovale, and severe hearing loss. A high-resolution chromosome analysis (550 band level) including a FISH probe study for the 22q11 deletion was normal. At nine months of age, the patient had significant feeding difficulties. Height, weight and head circumference was below the third percentile. His developmental milestones were within normal limits. The above findings are consistent with the diagnosis of OAFNS.

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Cervical spine anomalies in Weaver syndrome; a diagnostic clue in adults. T. E. Kelly. University of Virginia, Charlottesville.

Weaver syndrome was initially described as an overgrowth syndrome with advanced bone age and characteristic facies in two unrelated males (Weaver et al., 1974). Subsequent reports included only sporadic cases. More recently, autosomal dominant inheritance has been established (Fryer et al., 1997; Proud et al., 1998). In these multiplex families, the diagnosis has not been readily apparent in affected parents. This difficulty appears to be related to the evolving phenotype (Greenberg et al., 1989) and variability in expression with biased ascertainment. Anticipation may be operative, but analysis of additional families is needed to support this suggestion.

This reports describes affected half-brothers who manifest tall stature, advanced bone age, camptodactyly, characteristic facies, mild contractures of major joints and developmental delay. Their father, apart from tall stature (206.5 cm) had normal hands and facies and no joint restrictions. Photographs of the father as a child did not show facial features suggesting Weaver syndrome and he had had normal cognitive development as a child. However, all three had an element of cervical kyphosis and lateral films of the cervical spine demonstrated odontoid hypoplasia and anomalous development of C-3 in one brother, C-4 in the other brother and C-5 in the father. MRI's demonstrated stenosis of the cervical spine but no evidence of spinal cord compression. All three had broad femoral necks.

The proband in the family was diagnosed prenatally to have a sacro-coccygeal teratoma that was surgically removed neonatally. Two additional instances of tumors in children with Weaver syndrome are known to the author. These observations suggest that the underlying defect in Weaver syndrome may involve a growth factor which predisposes to tumor formation.

A collaborative effort is underway to map the Weaver syndrome gene. Additional families with this disorder are being sought for this project. Potential collaborators may contact the author at TEK8S@virginia.edu.

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Evaluation of telemedicine use for clinical genetics services in Iowa. K.M. Keppler-Noreuil[1], J. Welch[1], S. Sebille[1], J. Grigsby[2], S. Zollo[1]. [1]Univ. of Iowa Hospitals & Clinics, Iowa City, IA, [2]Univ. of Colorado, CO

Clinical genetics services in Iowa are delivered to 16 clinic sites with over 87 clinics/year by the Regional Genetics Consultation Services (RGCS)/ Univ. of Iowa, Dept. of Peds. Univ. of Iowa has an extensive telecommunications network, which connects 11 hospitals in Iowa using the interactive video system, TeleDoc with a digital exam camera, otoscope and electronic stethoscope. We recently completed a 15-month pilot project, which integrated the resources of Univ. of Iowa's telemedicine program with the RGCS to evaluate the use of telemedicine for delivery of clinical genetics services.

We evaluated the effectiveness of telemedicine for follow-up genetics visits by examining the following parameters: 1) patient satisfaction and compliance; 2) physician satisfaction and productivity, 3) utility (advantages and disadvantages) in different types of genetics consultations, 4) ease of use; 5) cost-effectiveness, and 6) access. These parameters were compared with the regular RGCS clinics. Each patient and his/her family, referring physician, consulting physician, and the genetic nurse counselor completed surveys regarding demographics, access, cost & satisfaction. Forty-seven patients were seen in 12 clinics. Attendance rate was 87% compared to 90% in RGCS clinics. The patient group included 24 males and 23 females. Ages ranged from 7 months to 37 years. Of the 47 patients, 36 (76%) had pre-established diagnoses; 11(23.1%) did not. Diagnoses included a variety of genetic conditions such as, chromosomal, single gene disorders, FAS, and MCA syndromes. Assessment of the suitability and clarity of telemedicine to visualize the many varied clinical exam findings was completed. The survey results revealed scores ranging from 3.62 to 3.92 on a 1-5 scale with 5 being excellent. Responses from patient satisfaction surveys showed that most families (44/47) were very satisfied with the health care they received and quality of telemedicine interaction. We also evaluated costs: one six-hour clinic was slightly less ($450) than the regular RGCS clinic (~$500), and was similar to other telemedicine clinics held at UIHC (avg. cost $487), excluding physician professional fees. Potential advantages of telemedicine included similar clinical productivity for number of patients seen per time slot, but elimination of travel time to and from the clinic site, and ability of physician to complete work/answer calls. Potential disadvantages included occasional interruptions in transmission, inability to palpate or completely assess neurological exam, and time to adjust camera position. We will review further survey results and demonstrate the quality of the transmission