

1291

AUTOSOMAL DOMINANT INHERITANCE OF SPONDYLOLISTHESIS, SPONDYLOLYSIS AND ACROMIAL SKIN DIMPLES.

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Spondylolisthesis (SOL) which is a forward displacement of the vertebra and spondylolysis (SLY) which is a deterioration or fracture in the pars interarticularis of the vertebral arch often occur together with SLY usually giving rise to SOL. These defects often involve the 5th lumbar vertebra and have an increased association with spina bifida occulta of 5th lumbar vertebra and the 1st sacral vertebra. Symptoms usually begin in late adolescence or young adulthood and include back spasm, back pain, sciatic pain, and spinal curvature. Autosomal dominant inheritance (Clin Genet 13:471,78) has been noted in some families.

Acromial skin dimples (ASD) are rare in normal individuals, but can be found in conditions where there is a deficiency of subcutaneous fat, muscle, and/or bone. Two families (Amer J Hum Genet 26:412,74 and Amer J Med Genet 6:259,80) of otherwise normal individuals have been reported with autosomal dominant ASD. No family has been reported with SLY, SOL and ASD.

The present report identifies a 4 generation family of 9 affected persons with SOL and SLY. In those individuals personally examined (4), the presence of ASD is segregating with SOL and SLY. Additionally, the dimples are congenital and are associated with decreased shoulder muscle mass. The uniqueness of this association will be discussed and the potential value of recognition of ASD as a presymptomatic marker for SOL and SLY in the children of affected adults.

1292

PREDICTING BIRTH WEIGHTS FROM TRACE ELEMENTS IN MATERNAL SERUM AND AMNIOTIC FLUID. Gene S. Hall and Ming-liang Lee (spon. by L.T. Taft), UMD-

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The concentrations of 22 elements (K,Ca,V,Cr,Mn,Pb,Ag,Zn,Fe,Cu,Rb,Ba,Al,Sr,Mg,Na,Sn,P,Ti,B,Ni,Co) were quantitatively determined in 88 pairs of maternal serum and amniotic fluid that were obtained simultaneously at 16-19 weeks gestation. The concentrations were determined by direct current plasma - atomic emission spectrophotometry (DCP-AES). A follow up of the 88 patients was made to obtain the birth weight, length and head size of their infants. Using concentrations of the element and the ratios of the element in maternal serum to that in the amniotic fluid as the independent variable, and physical parameters of the infants as the dependent variable, a set of multivariable equations was derived. The best equation ($r=0.70$) for predicting the birth weight was found

to be: birth weight (gm) = $200 \left(\frac{Z_S}{A_{AF}} \right) + 260$, where Z_S and

A_{AF} represents concentration of Zn in maternal serum and amniotic fluid, respectively. Similarly, but to a lesser extent, the ratio of Fe in the maternal serum to Fe in the amniotic fluid accounted for 60% of the variance ($r=0.60$) in the birth weights. Several other equations will be presented as well.

1293

FORAMEN OVALE ATRIAL SEPTAL RATIO: EVIDENCE FOR DIFFERENT PATHOGENIC MECHANISMS IN CONGENITAL HEART DEFECTS

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Foramen ovale atrial septal ratio in-utero is directly proportional to transatrial blood flow. We now studied FO:AS in defects with VSD or intact ventricular septum (IVS) to ascertain patterns of intracardiac blood flow. Included were 11 normal hearts, 12 isolated perimembranous VSD, 8 coarctation of the aorta (COA) IVS, 10 COA with VSD, 6 type B interrupted aortic arch (IAA), 4 pulmonary atresia IVS, 7 pulmonary atresia VSD, and 10 tetralogy of Fallot. From planimeter measurements of atrial septal and foramen ovale area, we calculated FO:AS. These data presented as $x \pm SD$ were analyzed by ANOVA.

The area of the atrial septum was similar among the groups. FO:AS ratio were: normal heart .24 \pm .07; isolated VSD, .40 \pm .06; COA IVS, .15 \pm .07; COA VSD, .34 \pm .07; IAA, .36 \pm .12; pulmonary atresia IVS, .38 \pm .10; pulmonary atresia VSD, .11 \pm .08; tetralogy of Fallot .19 \pm .06.

Thus, defects with intact ventricular septum are associated with a predictable variation in FO:AS ratio suggesting that hemodynamics are an important pathogenetic mechanism in these defects. Conversely, defects with VSD have a discordant FO:AS ratio suggesting that other mechanisms such as abnormal conotruncal septation may be the primary abnormality. These results emphasize the defects classified by anatomic similarities may have different pathogenic mechanisms.

1294

ORAL ETHER LIPID THERAPY IN PATIENTS WITH ZELLWEGER SYNDROME OR ZELLWEGER-LIKE DISORDERS. Ronald D.

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Patients with the cerebrohepatorenal syndrome of Zellweger (ZS) lack peroxisomes and certain peroxisomal enzymes such as dihydroxyacetone phosphate acyltransferase (DHAP-AT) in their tissues. Deficiency of this necessary enzyme for glycerol ether lipid biosynthesis provides a biochemical criterion for diagnosing patients with more subtle alterations of peroxisome function and suggests a therapeutic strategy for ZS patients. We describe the oral administration of an emulsion of alkyl glycerols to two patients with ZS--one with classic manifestations and 9% of control fibroblast DHAP-AT activity, the other with 30% of control fibroblast DHAP-AT activity and milder disease. Case 1 had classic ZS and received oral ether lipids during intervals from age 4 months to her death at age 10 months. Case 2 had hypotonia, peripheral retinal pigmentary changes, hepatomegaly, developmental delay with minimal dysmorphic features and has received oral ether lipids from age 15 months to his present age of 20 months. In case 1, treatment produced a qualitative increase in erythrocyte plasmalogens but little evidence for clinical benefit. In case 2, dramatic improvement in muscle strength and vision were noted after instituting therapy. These results suggest the need for controlled evaluation of glycerol ether lipid therapy in selected patients with peroxisomal disorders.

1295

FETAL PRIMIDONE EFFECTS. H. Eugene Hoyme and

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The incidence of major malformations in the offspring of epileptic women is approximately 2-3 times that of the general population. The delineation of recognizable patterns of malformation associated with specific drug exposures *in utero* implicates drug therapy as a major causative factor. Review of the literature and recent evaluation of 3 children with intrauterine primidone exposure reveal a distinctive pattern of malformation secondary to primidone, i.e., fetal primidone effects.

The 3 affected children include an 18-month-old Hispanic boy and 2 white half siblings, a 13-year-old girl and an 8-year-old boy. In each case the mother took primidone daily throughout gestation. There was no family history of mental retardation or birth defects. The pattern of malformation was remarkably similar among the 3 children reported here and previous cases from the literature. Features include: developmental delay, ptosis, midfacial hypoplasia, flat nasal bridge, epicanthus, telecanthus, short nose with anteverted nares, and 5th finger clinodactyly. Variable features include: seizures, hearing loss, upslanting palpebral fissures, unusual hair patterns, and short 5th metacarpals and/or metatarsals.

Data from these patients indicate that maternal primidone intake during gestation may be associated with a recognizable pattern of malformation in exposed offspring.

1296

FETAL ORIGIN OF MATERNAL SERUM ALPHA-FETO-PROTEIN (AFP) DEMONSTRATED BY DNA-RNA HYBRIDIZATION. R. Gordon Hutcheon, Harold M.

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Recent retrospective studies have shown a correlation between low maternal serum AFP levels and the presence of a fetus with an autosomal trisomy. The amniotic fluid AFP levels in these pregnancies tend to be decreased. A possible explanation for the low maternal serum AFP is that the trisomic fetus produces less AFP and/or impairs placental transport of AFP. Alternatively, the AFP in maternal serum might represent endogenous production in response to a fetal signal (re-activation of the previously repressed AFP gene) and the defective trisomic fetus is unable to provide an adequate signal. This study was undertaken to examine the contribution of the maternal liver to the AFP that appears in the maternal serum during pregnancy. Total RNA was isolated from the livers of pregnant, non-pregnant, and fetal mice. Northern blots were prepared and probed with cDNA for mouse AFP and rat albumin mRNA. The albumin probe hybridized well with all samples whereas the AFP probe hybridized only with the fetal liver RNA. The results are consistent with the widely held notion that maternal serum AFP is entirely of fetal origin. Decreased maternal serum AFP associated with a trisomic fetus may contribute to an increased risk for fetal demise, pregnancy loss, or other adverse outcome.