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MIDTRIMESTER DIAGNOSIS OF OSTEOGENESIS IMPERFECTA, TYPE 2, Nuhad D. Dinno, Uraib Yacoub, James F. Kadlec and Kenneth L. Garver, (Spon. by Billy F. Andrews), University of Louisville School of Medicine, Departments of Pediatrics, Pediatric Pathology & Radiology, Louisville, Ky., Magee Women's Hospital, Department of Reproductive Genetics, Pittsburgh, Pennsylvania.

We report two affected offspring with Osteogenesis Imperfecta, Type 2. The first child was born near term and expired shortly thereafter. Prenatal radiologic examination was consistent with O.I., Type 2. The second affected fetus was diagnosed at 19 weeks gestation by sonographic and radiographic imaging even though the amniotic fluid pyrophosphate was negative at 14½ weeks gestation. The skull was poorly mineralized and compressed. Long bones were shortened, angulated, and markedly irregular. There was deficient ossification of the spine, extremities, and minimal patchy ossification of the calvarium. Pregnancy was terminated at 21 weeks following the radiographic diagnosis. Radiologic and pathologic examination of the abortus was consistent with the prenatal diagnosis.

Although the diagnosis of this, as well as other bone dysplasias has been made in utero during late pregnancy, we conclude that radiographic and sonographic imaging may be the only method of diagnosis of O.I., Type 2 during midtrimester gestation.

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THIAMINE RESPONSIVE MAPLE SYRUP URINE DISEASE, Louis J. Elsas, Deborah S. Lubitz, Paul M. Fernhoff, Phillip P. Dembure and Dean J. Danne, Emory Univ. School of Medicine, Dept. of Pediatrics, Atlanta, Ga.

Thiamine pyrophosphate (TPP) is a coenzyme of mammalian branched chain α -ketoacid dehydrogenase complex (BCKAD). We have previously reported the *in vitro* stabilizing effect of saturating quantities of TPP on this multienzyme complex (Arch. Biochem. and Biophys. 202:23, 1980). In this investigation, we study the *in vivo* response to thiamine of four children affected with Maple Syrup Urine Disease (MSUD), (CM, JP, TM^c and VH). Fasting plasma levels of the branched chain amino acids, α -ketoacids and the BCKAD activity in peripheral leukocytes were measured before and during four weeks of 200mg thiamine P.O. per day while maintaining identical diets. TM^c, VH and JP had significant falls in the mean blood values for all three branched chain amino acids ($p < 0.05$). Corresponding decreases in plasma branched chain α -ketoacids occurred in TM^c and JP, but not VH. CM exhibited no decrease in the measured parameters. The patients exhibiting a response (TM^c, VH and JP) had measured BCKAD activity in their peripheral leukocytes ranging from 3-10% of normal controls, while CM had enzyme activity less than 1% of the normal controls. These results indicate that some patients with MSUD will respond to supraphysiological thiamine supplements and that the ability to respond is associated with residual enzyme activity present. The mechanism postulated for this response is stabilization of the BCKAD enzyme complex when TPP binding sites are occupied. (Supported by NIH Grants HD 08388 & CRC 00039).

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EXPERIENCE IN THE PRENATAL DIAGNOSIS OF ARGININO-SUCCINIC ACID (ASA) URIA AND CITRULLINEMIA. Lynn D. Fleisher, Helen R. Salwen and Henry L. Nadler. Northwestern U. Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois.

Citrullinemia and ASA uria, which result from deficient activities of ASA synthetase and ASA lyase, respectively, are diagnosable *in utero*. Several laboratories have experienced difficulties with direct enzyme assay due to low activities of these enzymes in crude extracts of cultured amniotic fluid (AF) cells. Monitoring 4 at-risk pregnancies, with a microassay based on the incorporation of ¹⁴C citrulline and ³H leucine into protein *in situ*, has shown us that it is crucial for the proper control cell types to be used and grown in parallel with the at-risk cells. For example, control AF fibroblasts have a mean activity of 0.67 (¹⁴C/³H incorporated), whereas control AF epithelial cells have a mean of only 0.09. The importance of this distinction was made clear when we recently monitored a pregnancy at-risk for citrullinemia. The first cells to grow out were epithelial and had activity of 0.14. The culture later became fibroblastic and the activity rose to 0.7. Only when compared to their proper controls did both results indicate a normal fetus. We also have found that control and at-risk cells must be assayed at identical stages of confluence, since increasing activity is seen with increasing confluence. A 10-fold increase in the number of cells planted raised the activity in 2 of our control lines by 3 to 5-fold. Our experience thus indicates the critical need for precise control of tissue culture variables, and the advantages of the microassay system, for prenatal diagnosis of these disorders.

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THYMIC APLASIA IN SIBLINGS, Robert Forsythe (Sponsored by Grant Morrow), Ohio St. Univ. Coll. of Med., Cols. Children's Hosp., Dept. Peds., Cols., Ohio.

DiGeorge syndrome is usually reported as having occurred sporadically. This is the first report of the syndrome occurring in twins and only the second in family members.

Black male twins were delivered at 33 weeks gestation. They were dizygotic as proven by different blood types. Each developed hypocalcemic seizures at 9 days. The diagnosis of DiGeorge syndrome was made in each on the basis of refractory hypocalcemia, typical facial features, absent thymic shadow, congenital heart disease and repeatedly low T-cell rosettes with normal immunoglobulins. One died at 58 days of age of aspiration and congestive heart failure. He was found at autopsy to lack thymic tissue and parathyroids. His heart disease consisted of a hypoplastic ascending aorta with the right subclavian artery arising from the right pulmonary artery. The other twin, now 3 yrs. old, has serially low T-cell rosettes, normal PHA stimulation and normal immunoglobulins. He does not suffer from recurrent infections nor does he require calcium or parathormone supplementation. Clinically, he has a small VSD. He is now less than the 3rd percentile in both height and weight and is developmentally delayed. Maternal evaluation revealed normal calcium phosphorus and parathormone levels. Antilymphocyte antibodies were absent. Although DiGeorge syndrome is usually sporadic, the occurrence in nonidentical twins suggests a genetic etiology in this family.

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BIOCHEMICAL DEFECT OF NON-KERATAN-SULFATE-EXCRETING MORQUIO SYNDROME. Atsuko Fujimoto and Allen Horwitz. USC School of Medicine, Los Angeles, California and Department of Pediatrics, University of Chicago, Illinois.

Two children of second-cousin parents were found to have a very mild form of Morquio syndrome. A 14-year-old boy was 146 cm tall (<3rd%), and had fine corneal deposits in the eyes, a broad chest, dislocated hips, and flat feet. His 7-year-old sister had a broad chest, but otherwise normal physical development. An abnormal lumbar spine was seen in radiographs of both children.

Analysis of the urine from the affected children revealed a level of mucopolysaccharide about twice as high as that found in normal urine, but no evidence of keratosulfaturia. The majority of the mucopolysaccharide was chondroitin 6-sulfate. Multiple assays of N-acetylgalactosamine-6-sulfate sulfatase in leukocytes and cultured skin fibroblasts showed deficiency of this enzyme in the range found in the classical form of Morquio syndrome.

The disease described in this report resembles the non-keratan-sulfate-excreting Morquio syndrome described by McKusick (Heritable Disorders of Connective Tissue, 1972), although the present cases show a milder disease. To our knowledge, the biochemical defect of this form of Morquio syndrome has not been confirmed. This report identifies the enzyme defect of the non-keratan-sulfate-excreting Morquio syndrome. The report also demonstrates the absence of keratosulfaturia in a patient younger than 10 years of age with this disease.

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TRISOMY 20 MOSAICISM IN AMNIOCYTES WITH DELIVERY OF INFANT NORMAL SAVE FOR PUNCHED-OUT SCALP LESION. Lytt I. Gardner, Joseph T. Lamman, Jr., David O. Hakanson and Irwin E. Redlener. SUNY Upstate Medical Center, Dept. of Pediatrics, Syracuse and Slocum-Dickson Medical Group, Utica, NY.

A woman with strong history of endometriosis underwent amniocentesis because of age (37). Amniotic cell cultures done at the Birth Defects Institute, NYS Dept. of Health, showed 30% trisomy 20 cells in the first tap and 13% in the second tap (Harrison et al., Am J Human Gen 32:71A, 1980). At term an 8 lb 10 oz infant girl was delivered. She was clinically and neurologically normal except for a 1 cm area of denuded skin to the left of the midline in the occipital area, reminiscent of the scalp lesion of trisomy 13. By 6 weeks of age it had developed a raised cicatrix, as in trisomy 13 during "healing". Blood karyotype was 46,XX. Developmental milestones have remained normal to present age 16 months. Four normal live births have been previously reported after trisomy 20 mosaicism was detected in amniocytes (Am J Med Gen 2:365, 1978; Lancet 1:1089, 1980). At least 8 such pregnancies have been terminated, with 5 fetuses described as normal, 2 as dysmorphic and one not examined. Only in 2 cases have trisomy 20 cells been found in fetal tissues. Trisomy 20 mosaicism remains a troublesome finding in amniotic cell cultures. Whether the cells are due to cultural artifact (Harrison et al., *ibid.*) or are derived from early trophoblast (Warburton) or fetal renal tissue (Boué) is still an open question. The "trisomy 13" scalp lesion in the present patient seems hardly coincidental.