● 1201 CARDIAC MALFORMATIONS IN A/J MICE INDUCED BY PHENYTOIN

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The fetal hydantoin syndrome is characterized by unusual facies, increased incidence of cleft lip (CL) and/or palate, hypoplasia of the distal phalanges and an increased incidence of cardiac defects. The purpose of this study was to identify phenytoin as a cardiac teratogen in A/J mice and to identify the primordial cardiac structures affected. At 11 a.m. of gestational day 10, mothers of A/J mice were injected intraperitoneally with 75 mg/kg of phenytoin. Embryos, 24, 48, and 72 hours after such treatment, and newborn mice were sacrificed as were controls. The specimens were fixed in glutaraldehyde and dissected the following day. They were dehydrated in alcohol and dried by the critical point technique. The hearts were sputter coated with gold and examined with a scanning electron microscope at 20kv. 89/107 offspring of treated mothers had CL as compared with 8/135 controls. 49/89 were cyanotic at birth. 47 newborns had a patent ductus arteriosus. 44 had an ostium primum atrial septal defect, 11 with an associated cleft in the anterior mitral leaflet and 7 with clefts in the mitral and triscupid valves. Coarctation of the aorta was noted in 11/49 newborn mice. In conclusion, phenytoin can be embryopathic when the embryo is exposed during critical stages of development of the heart and facial processes.

1202 ABNORMAL GENITALIA IN MALES WITH SILVER-RUSSELL (SR) DWARFISM: A NOT INFREQUENT COMPLICATION.

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The patient to be described weighed 1210 gm at birth, with estimated (Dubowitz) gestation of 38 weeks. The mother had congenital hydrocolpos, hydronephrosis and bicornuate uterus. Length was 37 cm; head circumference 30 cm. There were hypoglycemia and thrombocytopenia in the neonatal period. The face was triangular, with the appearance of a large head and small chin, typical for SR dwarfism. The phallus was 2 cm long and was partially concealed by a rostral investment of scrotal folds. Testes were palpable bilaterally in the canals. Karyotype was 46,XY. Voiding cystourethrogram revealed a urethra with male configuration, as well as a 9 mm hypoplastic vagina posterior to the urethra. This is consistent with failure of Mullerian inhibiting factor to function in fetal life. Several patients with the SR syndrome have been found to have obstructive abnormalities of the GU system (Pediatrics 51:216, 1973). At 8 month follow-up the scrotum was almost flat, with only one testis barely palpable in the right canal. Literature review on both sexes with the SR syndrome revealed that 28% of documented cases were males with abnormal genitalia. Several reports described adequate masculinization at puberty. The latter finding is important to bear in mind when consideration is given to the possibility of assigning a female gender role if the penis is small.

● 1203 LONG-TERM EFFECTS OF MODERATE ALCOHOL CONSUMPTION DURING PREGNANCY.

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In order to study the effects of varying levels of alcohol consumption during pregnancy, a group of 1,529 unselected mothers were interviewed during their 5th month of pregnancy as to their use of alcohol. At birth, 82 of the infants born to drinking mothers were examined by a dysmorphologist, along with 81 controls (J Pediatr 92:457, 1978). In the current study, 75 of these infants were re-examined at 4 years, along with 130 children from the same study population. All exams were conducted without knowledge of the mothers' drinking history. Reported alcohol consumption during the month prior to recognition of pregnancy among mothers from the experimental group averaged 2.0 oz. absolute alcohol per day, while controls drank infrequently or never. 20% of the experimental group showed alterations of growth and morphogenesis compatible with some fetal alcohol effect, compared with 9% of controls ($p = .027$). There was an increasing incidence of recognizable alcohol effects with increasing alcohol consumption ($p = .013$). Of 11 children judged to show alcohol effects at birth, 10 of these were re-examined at age 4 years, and 8 were independently judged to show fetal alcohol effects; their mean IQ was 92. These data suggest that moderate alcohol consumption during pregnancy may result in specific lasting phenotypic alterations which can permit valid, reliable judgments as to the presence of fetal alcohol effects.

● 1204 DETERMINANTS IN THE MORPHOGENESIS OF MUSCLE TENDON INSERTIONS.

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Recent studies suggest that muscle originates from somites and tendons from lateral plate mesoderm. This study explored the factors which normally determine the location and insertion of a muscle, a previously unanswered question. Human experiments of nature with early problems in morphogenesis were used to determine how muscle development proceeds when known critical developmental factors are varied. In a variety of monozygotic conjoined twins for whom there could be no genetic determinants for muscle attachments at the sites of juncture, these attachments must follow general principles of morphogenesis. A second type involves absence of bone that antedated muscle and tendon development (e.g. radial aplasia). A third category includes mechanical alteration of early limb position prior to development of muscle attachments (e.g. early amnion rupture sequence). The dissection findings from all 3 types strongly imply a general hierarchy of muscle tendon attachments. Tendons appear to attach preferentially to bone. If the bone they would normally attach to is absent, they will attach to the next closest bone. If no such bone is available, they will attach to tendons, and if no tendon is available, occasionally they will attach to the aponeurosis of another muscle. If there is no connective tissue attachment site, there will be no muscle, implying a need for function in the development and preservation of muscle.

1205 THE STILLBORN INFANT: NEED FOR PEDIATRIC CONSULTATION.

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About 1 percent of pregnancies result in a stillborn infant. Thorough obstetric - pathologic - pediatric/genetic evaluation of 37 stillbirths showed a multitude of causes: maternal preexisting disorders (5%), maternal disorders of pregnancy (5%), disorders of placenta and fetal membranes (10%), umbilical cord abnormality (3%), fetal abnormalities (49%), and instances of sudden fetal death syndrome without specifically determined cause (27%). Frequently (76%) the cause was not obstetric and often (43%) it was not apparent from postmortem examination. Since the pathologic findings, where noted, generally related to fetal rather than to maternal abnormalities, the obstetrician may not be adept at delineating all the possible implications important for parental understanding and acceptance of the event, future obstetric management, recurrence risk determination, and selection of prenatal diagnostic procedures during future pregnancies. We recommend that obstetricians involve pediatricians (who may have to be better trained in this area!) as consultants to help determine the cause and implications of the event.

● 1206 ACROMESOMELIC DYSPLASIA, A HISTOCHEMICAL STUDY OF THE ENDOCHONRAL GROWTH PLATE,

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Endochondral growth plate cartilage from a patient with the typical clinical and radiographic features of acromesomelic dysplasia was studied histochemically and immunohistochemically. The investigation revealed many previously undescribed abnormalities. The cartilage was hypercellular in general. There were numerous small areas of matrix degeneration scattered through the resting zone and a few large islands of hypertrophic cartilage in the growth plate region. Staining indicated excessive amounts of chondroitin sulfate and an absence of collagen fibers in both of these areas. In the remaining cartilage, collagen fibers tended to aggregate around the cells. The resting chondrocytes were irregular in size and distribution, and many exhibited protein containing cytoplasmic inclusions. The growth plate per se was poorly organized; hypertrophic chondrocytes were randomly oriented. The provisional calcification of cartilage matrix was absent, but the mineralization of subchondral bone appeared normal except along the outer margin where bone formation extended into the perichondrial space. These abnormalities appear to be distinct for acromesomelic dysplasia. Moreover, they provide several clues regarding the pathogenesis of the disorder.