1303 CORRELATION BETWEEN PARIETAL HAIR WHORL LOCATION AND BRAIN DOMINANCE. Robert W. Marion (Spon. by H.M. Nitowsky) Albert Einstein College of Medicine, Bronx, New York 10461.

The parietal hair whorl represents the surface point under which maximum brain growth occurs between the 10th and 16th weeks of fetal life. Aberrations of the hair whorl's position have been observed in children with conditions such as primary microcephaly, in which there is abnormal growth of the brain during the early fetal period. In an attempt to determine whether parietal hair whorl position is a marker of brain dominance, we examined 50 staff members of the Pediatric Department of the Albert Einstein College of Medicine. All subjects were neurologically normal and free from birth defects. 37 (74%) were right handed, 10 (20%) were left handed, and 3 (6%) considered themselves ambidextrous. Right handed individuals were significantly more likely to have their hair whorl to the left of the midline than were non-right handed subjects (26 of 37 right handed people, or 70.3% vs. 2 of 13 non-right handed, or 15.4%, $p < .001$). Similarly, left handed subjects were significantly more likely to have a right-sided hair whorl than were non-left handed people (6 of 10 left handed subjects, or 60%, vs. 5 of 40 non-left handed, or 12.5%, $p < .001$). In conclusion, we have demonstrated a correlation between position of the parietal hair whorl and handedness suggesting that brain dominance is determined during the first 16 weeks of gestation. This finding may be helpful in predicting handedness in infants, and in the evaluation of children with developmental disabilities and craniofacial defects.

†1304 MEGALOURETHRA-A MINI EPIDEMIC? McGillivray, B.C., Clinical Assistant Professor, Department of Medical Genetics, University of British Columbia, Vancouver, B.C., Canada.

Megalourethera is a congenital abnormality secondary to abnormal formation of erectile tissue of the penis, not primarily a problem with the urethra. In the complete (fusiform) type all erectile tissue is involved leading to massive dilatation of the penis. In the incomplete scaphoid form the deficiency is limited to the corpus spongiosum associated with ballooning of the terminal portion of the urethra. In a short period of time, four infants were referred to the service with a fusiform lesion, in three leading to a massively dilated phallus. Three of the four infants had other associated abnormalities reminiscent of the VATER group. The abnormalities included TE fistula, vertebral anomalies, radial hypoplasia, and absence of thumb. Other than season of year, there were no significant features of family history or pregnancy history suggesting a particular teratogen. Although thirty cases described in the literature had megalophallus, only six were secondary to a fusiform lesion. Four of the six had a constellation of abnormalities similar to our infants. It is therefore important to differentiate the causes of megalourethra as the fusiform type is often associated with other abnormalities, and may well be a lethal condition.

●1305 FIRST TRIMESTER MATERNAL SERUM ALPHA-FETOPROTEIN (MSAFP) SCREENING. Aubrey Milunsky, Jack R. Wands, Dominique Bellet, Dept. Pediat., Boston Univ. Sch. Med. & Boston City Hospital., Div. Gastroenterol., Dept. Med., Mass. Gen. Hosp., Harvard Med. Sch., & Instit. Gustav-Roussey, Villjuif, France.

Second trimester MSAFP screening is valuable in the prenatal detection of neural tube defects and in the recognition of other problems. Our screening leads to amniocentesis in 1:400, but not infrequently leads to a later conclusion of prenatal studies with options to abort often between 20-24 wks. DB has established an extremely sensitive "simultaneous-sandwich" radioimmunoassay (M-RIA) with polystyrene beads coated with anti-AFP monoclonal antibodies and using solid phase support. Comparative assays to available polyvalent commercial kits showed M-RIA to be 4-10 times more sensitive. In addition, inter- and intra-assay variation and reproducibility were assessed over a wide range of values. Results were noted to be accurate with a coefficient of variation $< 5\%$. MRIA studies of 400 non-pregnant females showed serum AFP undetectable in 99.6%, others having MSAFP values < 3 ng/ml. We have analysed 449 first trimester MSAFP samples, from apparently normal pregnancies. We report that AFP was detectable between 8-9 wks, significant ($p < 0.001$) AFP "elevations" were noted at 10 wks, AFP rose linearly 10-24 wks, SEM's were small, higher AFP levels were found & M-RIA was accurate, precise, & reproducible. 3/4 patients have also had a 2nd trimester MSAFP screen. Correlations between ultrasound studied pregnancies, 1st and 2nd trimester AFPs, and outcome will be presented. These preliminary data suggest that MSAFP screening may be possible earlier than 16 wks and even in the 1st trimester.

●1306 NEURAL CREST INVOLVEMENT IN MOUSE TRISOMY 16 EMBRYOPATHY. Michael Msall, Mary L. Oster-Granite, and John Gearhart (Spon. by John W. Littlefield), Johns Hopkins University School of Medicine, Developmental Genetics Laboratory, Department of Pediatrics, Baltimore.

Murine Trisomy 16 (Ts16) has been proposed as an animal model for Down Syndrome. We examined serial histologic reconstructions of Ts16 fetuses from day 14 through 18 gestation. We found that 94% (N=52) of Ts16 mice had cardiovascular malformations. Endocardial cushion defects were most common (62%) and were associated frequently with conotruncal abnormalities (DORV, 36%; overriding aorta, 35%; PTA, 6%; TGA, 2%)

We found thymic hypoplasia in > 90% of Ts16 mice. Consistent with previous observations (Oster-Granite et al., Ped. Res. 17: 300A (1983)), we found facial, basiocciput, and audiovestibular (otic) abnormalities. In reconstructions of the temporal bones, no specimen showed more than 1.5 turns of the cochlea by day 18 (N=2.5).

Kirby et al (Science 220: 1059-1061 (1983); Science 223: 498-500 (1984) demonstrated in chick-quail chimeras the cephalic neural crest contribution to thymus development and to aorticopulmonary septation. The combination of cardiac defects, thymic hypoplasia, auditory, and craniofacial malformations we have observed in the Ts16 mouse is consistent with a generalized rhombencephalic neural crest deficiency. This deficiency may be due to failure of cell proliferation or migration, to excessive cell death, or to abnormal cell-cell interactions.

1307 HEARING LOSS AND NEUROLOGIC IMPAIRMENT: TIMING OF SYSTEMIC INSULT AS INDICATED BY TOOTH DEFECTS. Gail S. Murray, David C. Johnsen (Spon. by M. Hack) Case Western Reserve University, Dept. of Pediatrics, Cleveland.

Hearing loss and primary tooth defects have been separately associated with neurological impairment, but have not been systematically examined in the same population. To investigate the association of these defects and to explore their potential use as prenatal biological markers, 18 children presenting for hearing evaluation were examined. 11 had enamel defects. 5 had defects consistent with a systemic insult occurring in the 2nd trimester, 2 between 29-33 wks gestation, and 4 near term. Hearing loss was more severe in the 5 with enamel defects occurring in the mid-trimester ($\bar{x}$=70 dB), than in the 4 subjects with defects occurring around term ($\bar{x}$=23 dB) ($t=3.1$; $p<.05$). Of the remaining two subjects, one had normal hearing and the other had a moderate loss. A correlation was found between the average degree of hearing loss (in dB) vs. the estimated time of systemic insult (in wks gestational age) as indicated by position of tooth defect ($r=-.78$; $p<.01$). Neurological profiles also differed. Developmental delay was more prevalent and more marked in the group with defects occurring in the mid-trimester vs. term; 4/5 children in the former group had visual/occulomotor defects compared to none in the latter group. These findings suggest a differential susceptibility for developing neurologic structures such that a given systemic insult occurring in the mid-trimester of pregnancy appears to have more serious ramifications regarding subsequent auditory and neurologic function, than those occurring late in gestation.

1308 DEVELOPMENT OF THE HIPPOCAMPAL FORMATION IN TRISOMY 16 MICE. Mary L. Oster-Granite and George Hatzidimitriou (Spon. by John W. Littlefield). Johns Hopkins University School of Medicine, Developmental Genetics Laboratory, Departments of Pediatrics and Neuroscience, Baltimore.

Studies of the neuroanatomic features of murine trisomy 16 (Ts16), an animal model for human trisomy 21 (Ts 21, Down Syndrome), have focussed upon the structural and ultrastructural characteristics of germinative cells within the hippocampal formation. We prepared 5 micron plastic section serial reconstructions of the hippocampal formation of Ts16 and normal littermates from days 12 through 18 gestation.

We analyzed the sections morphometrically to determine the longitudinal extent of the hippocampal formation, its volume, and its cell density. All were reduced. In Ts16 mice, the overall shape of the hippocampal formation was distorted, and the appearance of the anlagen of the dentate gyrus was delayed as much as 48 hours. The shape of the lumen of the lateral ventricle was abnormal. In normal mice, the lumen shape was that of an open crescent at day 13; the shape became slit-like by day 15. In contrast, the shape of the ventricular lumen in Ts16 mice remained open and triangular at day 15 gestation.

In sections reembedded for ultrastructural analysis, we found reduced cell density and increased extracellular space in the Ts16 conceptuses. Synapses were not observed in either Ts16 or normal mice at these ages. The neuroblasts in both Ts16 and normal mice were indistinguishable morphologically.