1219 SPECIFIC DIAGNOSES AND PROGNOSES IN SGA INFANTS. David W. Smith, Mary Ann S. Harvey, Becky S. Bunn and John M. Graham. University of Washington School of Medicine, Department of Pediatrics, Seattle.

Of 1350 babies born at Group Health Hospital there were 4% who were 2SD or more down for gestational age in length, weight and/or head circumference. Each was examined to determine a specific clinical diagnosis and postnatal growth was followed. The most common diagnosis was maternal uterine constraint in 18(33%). 50% of the constraint babies had deformations beyond growth deficiency. These babies showed catch-up growth in the first month and complete by 2-6 mos. The second most common cause (16%) was heavy cigarette smoking. Only 6 of these 9 babies showed catch-up growth within the first 6 months. 9% were genetically small babies of small parentage and they did not show postnatal catch-up growth. There were 2 to 3 cases each of placental insufficiency, pre-eclampsia, a small MZ twin with A-V placental shunt, and a family history of SGA babies. Within these categories all showed catch-up growth except one of the MZ twins. 7 had malformation disorders and none of the 4 survivors showed catch-up growth.

Thus SGA is a non-specific feature which may be secondary to a host of different causes. The prognosis relates to the specific diagnosis. For the most common type of cause, late fetal uterine constraint, the prognosis for catch-up growth is excellent, The second most common, and most preventable cause, is heavy cigarette smoking, for which the prognosis is variable.

1220 THANATOPHORIC DWARFISM AND THE CLOVERLEAF SKULL, Anne-marie Sommer and Arthur J. Vaughn (Spon. by Stella B. Kontras). The Ohio State University College of Medicine, Department of Pediatrics and Children's Hospital, Columbus, Ohio.

The combination of both thanatophoric dwarfism and cloverleaf skull has been reported rarely although each condition separately has been well described. These conditions did occur in a patient who was born to young parents which was the only known case in the family.

J.C. was born to a 25 year old Gravida I Para I mother. Multiple anomalies present at birth were: the cloverleaf skull, flat facial features, mild proptosis of the eyes, ears located in the horizontal position, a very small thorax, protuberant abdomen with palpable liver and spleen and very short and bowed extremities with trident shaped hands and stubby feet. The weight was 3.69 kg, length 49.5 cm. and head circumference 36 cm. The baby was extremely hypotonic and expired at 17 days of age. X-rays revealed hypoplasia of the facial bones, pronounced lateral parietal bulges and upward protrusion from the frontal region of the skull and a CT scan revealed generalized hydrocephalus. X-rays of the extremities revealed shortened and bowed long bones and ribs which were described as short with a limited chest cage capacity. The post-mortem examination confirmed the clinical findings. Also, there was a left choanal atresia and an ostium secundum defect. There was marked disorganization of bone and cartilage at the growth plate showing severe irregularity at the epiphysis.

This case is reported because of the paucity of cases like this in the literature and the family's need for genetic counseling.

● 1221 MECHANISM OF DEXAMETHASONE-INDUCED CLEFT PALATE IN RATS: INHIBITION OF PROSTAGLANDIN AND THROMBOXANE SYNTHESIS IN FETAL PALATES IN VIVO. Georgia G. Tzortzatou and Allen S. Goldman. The Children's Hospital of Philadelphia & Department of Pediatrics, University of Pennsylvania, Philadelphia, PA 19104

We have hypothesized that the teratogenic mechanism of glucocorticoids involves the same biochemical pathway as the mechanism of their anti-inflammatory hormonal action, i.e., inhibition of arachidonic acid release and of prostaglandin (PG) and thromboxane (TX) production. Arachidonic acid reversed the production of cleft palate in rats by dexamethasone and this reversal was blocked by indomethacin, an inhibitor of PG and TX synthesis (cyclo-oxygenase) (Fed. Proc. 3616:955, 1980). Pregnant rats were treated with dexamethasone 3.75mg/kg or vehicle on days 12 to 15 of pregnancy, a regimen giving about 80% cleft palate. Three hours after the last dose of steroid on day 15 fetuses were removed by c-section and palates from each litter were dissected, pooled, sonicated, and incubated at 37°C for 3 hours. 100µl aliquots were removed at 1 hr. and 3 hrs. and the reaction stopped with 1ml ethanol. Aliquots of the ethanol extracts were measured for PG and TX by radioimmunoassay. PG and TX synthesis was proportional to time of incubation. Dexamethasone inhibited significantly the production of F2α, E2, 6-keto F1α, and TX B2 by fetal palates to about 50% of control values. Thus, evidence has been presented for the precise biochemical mechanism of glucocorticoid-induced cleft palate.

1222 FETAL GROWTH IN DRUG DEPENDENT PREGNANT WOMEN: QUANTITATIVE ASSESSMENTS. Ronald J. Wapner, R. Douglas Ross, Jack M. FitzSimmons, Martha E. Rudrauff, and Loretta P. Finnegan. Thomas Jefferson University Hospital, Departments of Obstetrics/Gynecology and Pediatrics, Philadelphia.

The association between maternal drug abuse during pregnancy and incidence of low birth weight (LBW) has been reported. However, intrauterine growth patterns and type of growth failure have not been delineated. This study was designed to explore the onset, type and etiology of growth failure. Fetal growth of 99 passively drug exposed fetuses was measured throughout pregnancy using ultrasound. Total intrauterine volume (TIUV), biparietal diameter (BPD), head circumference (HC) and abdominal circumference (AC) were measured. Results revealed that: all TIUV's and BPD's of the 86 appropriate for gestational age infants were within normal range; 21% of infants were LBW; 8% premature; 13% small for gestational age (SGA). Of the 13 women who delivered SGA infants, 11 had initial TIUV's >1 standard deviation (sd) below the mean; 7 of 8 studies at <24 weeks gestation already showed abnormal TIUV's. All 13 scans showed a BPD below the mean for gestational age; 11 of these were >2 sd's below the mean; the HC/AC ratios fell within normal range. Drugs of abuse were reviewed. Although pentazocine users constituted only 9% of patients studied, their infants represented 54% of the SGA infants. These data suggest: 1) early onset symmetrical intrauterine growth retardation is seen in drug dependent women; 2) pentazocine has a high potential for causing SGA infants, through a direct rather than an environmental effect.

1223 MATERNAL INSULIN: AN UNLIKELY FETAL TERATOGEN. John A. Widness, John B. Susa, William Oh and Allen S. Goldman; Depts. of Pediatrics, Brown University, Providence, RI, and Univ. of Pennsylvania, Philadelphia, PA.

The pathogenesis of congenital anomalies which are frequently observed in infants of diabetic mothers remains obscure. One possibility is that maternal insulin (I) may cross the placenta and act as a teratogen. Although at term the placenta is a barrier to I, this process has not been examined during organogenesis. To study this question, tracer amounts of radiolabelled I (I^{131} or I^{125}) shown to contain 69-85% immunoreactive I were infused into 7 pregnant rats on day 12½ postcoitum (organogenesis: day 7-14) with a prime plus constant infusion. After 2 hrs maternal plasma and fetal and placental tissue were obtained. Plasma and tissue samples were analyzed for total radioactivity (TRA) as well as the radioactivity of the trichloroacetic acid protein precipitable fractions (TCA ppt). Significant TRA was achieved in maternal plasma at 2 hr: $3.2 - 3.4 \times 10^3$ and $3.9 - 5.8 \times 10^4$ cpm per 100 µl for I^{125} and I^{131}, respectively. The percentage of the TRA in the TCA ppt was 59±7% (M±SD). This fraction contains the immunoreactive insulin fraction in addition to insulin polypeptide fragments. Placental tissue (containing some maternal blood) and fetal tissue had mean TCA ppt counts (per 100 mg) which were only 5.7% (0.7 - 16.5, range) and 0.05% (0 - 0.19) of the TCA ppt counts in maternal plasma. Since the fetus is protected from maternal insulin by the placenta during the period of late organogenesis, it is unlikely that maternal insulin acts as a fetal teratogen.

1224 CRANIOFACIAL DEVELOPMENT IN THE ANGELMAN HAPPY PUPPET SYNDROME (AHPS). Charles A. Williams, Harold O. Enoch, Gregory J. King, Jaime L. Frias. University of Florida, College of Medicine, Department of Pediatrics, and College of Dentistry, Department of Orthodontics.

Cephalometric analyses were performed on five caucasian patients with AHPS to further investigate the craniofacial abnormalities observed in this disorder. The study included four females and one male ranging in age from 11 to 33 years. Analysis of twenty-two angular and linear relationships measured on lateral cranial radiographs demonstrated the following significant abnormalities: microcephaly, short anterior and posterior cranial base, mid-face retrusion and decreased vertical face height. The sella turcica, reported as being displaced in previous studies, was normal in configuration and position in all our cases. In addition, despite the fact that four of our five patients appeared clinically prognathic, all had normal mandibular length, width and shape. It was concluded that this relative prognathism was caused by upward and forward rotation of the mandible as a consequence of the shortening and retrusion of the mid-face. We postulate that these abnormalities, responsible for the characteristic craniofacial configuration in patients with the AHPS, result from the shortening of the anterior cranial base which is secondary to abnormal brain morphogenesis and growth.