†344 IS COCAINE A TERATOGEN IN HUMANS? Ben.K. Rajegowda, Rosila Lala, Anasuya Nagaraj, Veronica Stephan and Silvia Iosub. (Spon.by Harry S.Dweck) N.Y.Med. Coll-Lincoln Hosp.,Div.of Neon-Perin. Med.,Dept. of Peds., Bronx, N.Y.

Cocaine (C) is second only to marijuana (MJ) as a recreational drug in the U.S.A. To assess the teratogenicity of cocaine, we prospectively compared the prevalence of congenital malformations (CM) in 581 infants from 576 (DAM) drug abusing mothers (cocaine alone or with other drugs) with controls (8235 infants from 8180 mothers). Malformations were divided into major and minor.

	C	C+ MJ	C+Op- iates	C+ 'Other'	MJ	Opi- ates	A	No drugs Tot.	(Control)
CM Major	2	1	2	2	2	1	1	11	78
CM Minor	7	4	6	1	2	4	2	26	340
Normal	178	97	82	13	74	97	3	544	7817
Total	187	102	90	16	78	102	6	581	8235

Major CMs were higher when the combined data of all infants of DAMS (11/581) were compared to the controls (78/8235), (p=.04, chisquare test). The only other significant finding was the higher prevalence of CM in the C+ 'Other' (3/16) vs any other infants of DAMs as well as controls, (p <.05, Fisher exact test). No other increase in the prevalence of CM was found in infants of cocaine (alone or with other drugs) vs other substance abusers or controls. The total incidence of CM was similar for infants of DAMs vs controls. Further studies are needed to elucidate the teratogenic effect of cocaine and its derivatives on humans.

†345 SUPRAVALVULAR AORTIC STENOSIS WITHOUT WILLIAMS SYNDROME. Michael A. Schmidt, Virginia V. Michels, Robert H. Feldt, Donald J. Hagler, Gregory J. Ensing, Mayo Clinic, Depts. of Genetics and Pediatrics, Rochester, Minnesota; Guy A. Carter, Univ. of South Dakota Medical School, Dept. Pediatrics, Sioux Falls.

Supravalvular aortic stenosis (SVAS) is the major cardiac lesion of Williams Syndrome (WS). WS also has features of mental retardation (MR), characteristic facies and variable hypercalcemia in infancy. Most cases of WS probably represent new autosomal dominant (AD) mutations. Isolated SVAS ± peripheral pulmonic stenosis can occur sporadically, however, when reported to occur in more than one family member, it has been assumed by some (McKusick #19405) to be a mild expression of WS. This has major implications for genetic counseling, cardiac evaluation and for the prognosis of the patient and family.

We evaluated 21 members of a 3-generation, 34-member family in which 12 have SVAS documented by ultrasound (US). Four others have SVAS by report of cardiac US done elsewhere. The pedigree was compatible with AD inheritance with high penetrance and variable expression. In 5 tested individuals, the IQ ranged from 102-107; all other members were of normal intelligence by personal observation and interview. No family member had the characteristic facies or other associated findings of WS.

This family study, the largest studied to our knowledge, illustrates that isolated SVAS without WS can be inherited as an AD disorder. Although allelic heterogeneity can not be excluded, this family demonstrates that SVAS and WS are separate clinical entities. Relatives of patients with isolated SVAS should be evaluated for mild signs of disease, and families with SVAS can be reassured that occurrence of MR with WS is unlikely to occur.

346 PRENATAL PATHOGENESIS OF MACROORCHIDISM IN THE FRAGILE X SYNDROME. Lawrence R. Shapiro, Patrick L. Wilmot, Rawhi A. Omar, Marianna M. Davidian, and Praveen N. Chander, New York Medical College and Westchester County Medical Center, Departments of Pediatrics and Pathology, Valhalla and Letchworth Village, Thiells, New York.

Light and electron microscopy of fetal testes at 16 and 22 weeks of gestation, following prenatal diagnosis of the Fragile X Syndrome, revealed that the morphogenesis of the macroorchidism begins prior to 16 weeks and is progressive throughout gestation.

Light and electron microscopy of the testis at 16 weeks revealed interstitial edema with increase in interstitial ground substance associated with an increase in hydrophilic glycoprotein granules, scattered collagen fibers and bundles of microfibrils. At 22 weeks, there was progression of these changes with further increase in ground substance, collagen fibers grouped in bundles and a moderate increase in fibroblasts.

The primary mechanism of the macroorchidism appears to be fetal interstitial cell production of an abnormal ground substance comprised of glycoprotein granules which are hydrophilic and result in interstitial edema by at least 16 weeks. Thus, a primary connective tissue defect may be responsible for the macroorchidism as well as some of the other features of the Fragile X Syndrome.

●347 LACK OF EVIDENCE FOR CRANIO-FACIAL DYSMORPHISM IN CHILDREN WITH AIDS. Tariq M. Sheikh, Qutub H. Qazi, Senih Fikrig, Howard Menikoff. Dept. of Pediatrics, SUNY-Health Science Center at Brooklyn, New York.

We have evaluated 30 children with HIV infection ranging in age from 4-1/2 months to 8-1/2 years, and 30 controls matched for age, sex, and race/ethnicity for growth, head size, craniofacial dysmorphism, dermatoglyphics and other physical features. All patients and their mothers were serologically positive for HIV-antibody.

Clinical Features	Patients N=30	Controls N=30	χ^2	P
Growth Failure	13 (43%)	0 (0%)	11.368	0.001
Microcephaly	8 (26%)	0 (0%)	7.484	0.006
Prominent Forehead	11 (36%)	6 (20%)	1.248	0.263
Hypertelorism	5 (16%)	8 (26%)	0.676	0.584
Flattened Nasal Bridge	8 (26%)	16 (53%)	2.009	0.153
Upslanted eyes	1 (3.3%)	1 (3.3%)	0.517	0.521
Blue Sclera	3 (10%)	3 (10%)	0.183	0.672
Triangular Philtrum	4 (13%)	5 (16%)	0.227	0.640
Patulous Lips	6 (20%)	2 (6.6%)	1.958	0.158

Aside from growth failure and microcephaly (which are attributable to chronic infections and central nervous system lesions in AIDS patients) there were no significant differences in clinical findings (including dermatoglyphics) between patients and controls. A previous report describing craniofacial dysmorphism in children with AIDS noticeably lacked in comparison with normal controls. We conclude that although there is evidence for intrauterine transmission of HIV infection causing immunological impairment, there is no evidence for "embroypathy".

†348 INCONTINENTIA PIGMENTI (IP): LINKAGE ANALYSIS OF A KINDRED USING MULTIPLE Xp GENOMIC MARKERS. Daniel Sinnett, Grant Mitchell*, Léo Lavergne, Serge B. Melançon, Louis Dallaire, Michel Potier and Damian Labuda. Génétique Médicale, Hôpital Ste-Justine, Université de Montréal, Montréal, Québec, and *Department of Pediatric Genetics, Johns Hopkins University, Baltimore, MD.

IP (in McK 30830) is an inherited highly pleomorphic disease associated with central nervous system disorders in 30% of cases. It is transmitted in an X-linked dominant fashion with prenatal lethality in affected males. To date, we have used 17 probes to study genomic digests from members of a 3-generation pedigree which contains 13 potentially informative meioses. Informative polymorphisms were detected with five probes. Arranged from proximal to distal Xp, they are: p58-1 (which maps to Xp11→cen); OTC(Xp21); 754(Xp21.1→Xp21.2); pERT87-15(Xp21) and dic56(Xp22→Xpter). When we examined the segregation of these multiple loci with the IP phenotype we observed one instance of double recombination, 8 simple recombination events and 4 instances of no recombination. For p58-1 we documented 2 recombinants with respect to IP in 11 meioses (2/11). The values for the other markers were: OTC, 5/13; 754, 6/12; pERT87-15, 7/12 and dic56, 9/13. These data suggest that IP locus is in or below Xp11, and are consistent with the cytogenetic assignement of IP to Xp11 on the basis of IP patients who carry Xp11-autosome translocations (Hodgson et al. (1985) Hum. Genet. 71:231-239).

349 INCIDENCE OF CONGENITAL ANOMALIES IN A NEONATAL INTENSIVE CARE UNIT (NICU). Lourdes C. Sosuan, Emily Ling, Judith G. Hall. Pediatrics and Medical Genetics, B.C's Children's Hospital and the University of British Columbia, Vancouver, B.C., Canada.

A one-year study (1985) review showed a high proportion of infants with congenital anomalies admitted to the NICU of our perinatal center. Congenital anomalies were present in 79 (10%) out of 790 admissions.

Classification of the congenital anomalies fell into two groups. 1) Single defect (51%): Deformation-2; Malformation-38 (CSV 12, GU 10, Pulm.7, CNS 6, GI 3). II) Multiple anomalies (49%): Chromosomal-13; Monogenic-11, Unknown-15 (i.e. about 40% of the multiple congenital anomalies could not be diagnosed).

Clinical profile of these infants will be presented in percentage and compared to the overall NICU admission in brackets. 1) Gestational age, range 25-42 wks: preterm 73% [76%]; full-term 27% [24%]. 2) Intrauterine growth retardation in 22% [6%]. 3) Multiple births in 6% [16%]. 4) Fetal anomalies were suspected antenatally in 65%. 5) Delivery by cesarean section occurred in 43% [38%] and was performed primarily for fetal reasons in 74%. Of these, 64% had lethal congenital anomalies, chromosomal disorders or recognized syndromes with grave outcome. 6) Mortality in NICU was 25% [10%]; all of these deaths were attributed to congenital anomalies, none to prematurity. Another 10% [1%] died within the first year after discharge/transfer. 7) These cases accounted for 2580 patient-days (13% of NICU workload).

These findings raise concerns about the perinatal diagnosis and management of neonates with congenital anomalies, particularly those suspected antenatally.