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Serum Leptin Concentration and Lipid Profiles in Puerto Rican Bardet-Biedl Syndrome. A. Santiago-Cornier[1,5], W. Arias [2], R. Soto [2], J. Acevedo [3], S. Carlo[4], D. Valencia[5], L. Caban[6], T. Frazer[6]. 1 Dept. of Caban, Ponce Sch. Med., Ponce ,PR. 2 Dept. of Ped. Ponce Regional Hosp. 3 Dept of Nursing, Univ. of PR, Arecibo, PR. 4 Div of Genetics, Mount Sinai Hosp. NY. 5 Genetics Section, 6 Dept. of Pharm., Ponce Sch. of Med. Ponce, PR.

Bardet- Biedl syndrome (BBS, MIM#209900) is an autosomal recessive disease of unknown etiology that exhibits phenotypic and genetic heterogeneity. Characteristic clinical features includes retinitis pigmentosa, obesity, hypogenitalism, polydactyly, and mental retardation. We have studied 7 large inbred families in Puerto Rico (PR) with BBS and found linkage to chromosome 11 q locus. We performed physical and biochemical examinations on 21 patients (18 males, 3 females) and 244 family members. Evaluation included ophthalmology examination, renal/ liver ultrasound, renal function tests, and developmental assessment. All patients exhibited obesity, polydactyly, mental retardation and retina degeneration. Heterozygotes for the BBS (obligate carriers) exhibited a 67% rate of obesity, 58% rate of diabetes and 42 % rate of hypertension. Median Body Mass Index (BMI) of patients was 33.7kg/m^2 , 30.0kg/m^2 in heterozygotes (obligate carriers), and 29.6 kg/m^2 in family members with unknown genotype. To further investigate BBS we evaluated serum concentrations of leptin, cholesterol, triglycerides, low-density, and high-density lipoprotein levels on 11 patients and 56 family members including 12 obligate carriers. The mean leptin concentration was 39.3 ng/ml in patients. These patients average BMI was 30 kg/m^2 and presented leptin average of 136.7 ng/ml and a median of 136.7 in females and an average of 19.9 and median of 30.4 in males. Obligate carriers BMI media was 29.8 kg/m^2 and leptin concentrations showed a media of 15 ng/ml and a median of 16.3 ng/ml; five-fold less than affected patients although BMI were essentially the same. Normal leptin values for PR adolescents: males: 2.8 ng/ml ±1.1; females 13.6 ng/ml ± 3.1.

We conclude that leptin correlates with BMI in patients with BBS having a mean leptin concentration that is 8 fold higher than normal weight adolescents. Furthermore the ration of serum leptin in affected females to affected males is similar to the ration observed in normal adolescents. There is a 2:1 fold increase in females and a 3:1 fold increase in males obligate carrier of the BBS gene in comparison with obese females and males with similar age and BMI. We proposed that having the BBS-PR gene does predispose to higher leptin levels in comparison with controls.

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Genetic studies in the focal dermal hypoplasia of Goltz syndrome. RE Schnur, LA Reed, KA Mockridge, M Gao. Cooper Health System/Univ. of Medicine and Dentistry of NJ, Camden, NJ.

The focal dermal hypoplasia of Goltz (FDH) syndrome is an X-linked disorder with skin, skeletal, and ocular defects. The FDH phenotype shares features with the microphthalmia with linear skin defects (MLS) syndrome, which is associated with deletions of Xp22. Familial cases of FDH are rare; no genetic studies were performed previously. We studied linkage to twelve polymorphic markers between *DXS43* and *OA1* in an FDH family, including an affected mother (FDH7), her husband, affected daughter (FDH8), and unaffected son. Phenotypically, the mother's findings were limited mostly to the skin. Her karyotype was normal, 46, XX. She had patterned telangiectatic streaks, atrophic areas, scalp aplasia cutis congenita, perianal papillomas, and subepidermal lipomatosis. Her ocular exam was normal; there was no evidence of osteopathia striata on knee radiographs. Dentition was normal except for multiple caries and some grooving at the edges of her molars. Breasts were symmetric; nails were relatively normal. Her 12 year old daughter has normal growth and development, similar cutaneous lesions, including scalp aplasia cutis congenita, an atrophic erythematous area of the face, hyper-and hypopigmented areas, multiple dystrophic nails, grooved surfaces of her teeth, high palate, mild scoliosis, 3-4 finger syndactyly, and 2-3-4 toe syndactyly. X-inactivation/methylation analysis of FDH7 and FDH8, and six other FDH patients was performed in DNA from peripheral blood. FDH7 showed a skewed methylation pattern at the *AR* locus. FDH8 also showed skewed methylation at the *AR* and *MAOA* loci, but had a random pattern at the *DXS16* locus, which lies closer to the MLS critical region. Methylation patterns along the X-chromosome were also not homogenous in the other patients with FDH and did not correlate with phenotype severity. FDH7 was heterozygous at *DXS43, DXS1053, DXS1224, DXS7104, DXS7109, DXS1043, KAL,* and *OA1*. At each locus, her children inherited different maternal alleles. Thus, although limited, our linkage analysis is consistent with mapping of the FDH syndrome to the MLS critical region in Xp22.

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Typical "soup kid" facies of Albright Hereditary Osteodystrophy in early infancy and natural history of the phenotype through old age. L.R. Shapiro[1,2] and H. Taska.[2] [1]New York Medical College and [2] Westchester Medical Center, Valhalla, New York.

Albright Hereditary Osteodystrophy is characterized by short stature, obesity, rounded facies, shortened metacarpal and/or phalangeal bones, developmental delay/mental retardation and hypocalcemia in some forms which can be symptomatic.
In 5 patients, a typical facies was identified with round shape largely due to remarkably full cheeks, flat midface, depressed nasal bridge and upturned nose. During infancy the cheeks and face are reminiscent of a "Campbell Soup Kid," and the round shape and fullness of the cheeks persist through early childhood. By late childhood, the face remains round and full, but the remarkable fullness of the cheeks subsides and the "soup kid" facies becomes less apparent.
Undiagnosed older patients are usually evaluated because of a family member's concern about risks for mental retardation. Older affected individuals are short and obese and have small hands and feet with a round face. Review of photographs during infancy and childhood indicate the characteristic facial appearance and enable confirmation of the diagnosis.
Early diagnosis with prompt intervention or accurate diagnosis in later years is desirable and allows for appropriate genetic evaluation and counseling.

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Prenatal diagnosis of Smith-Lemli-Opitz syndrome via an abnormal maternal serum screen. M.B. Swing[1], G. Hirata[1], K.M. Gibson[2], R. Steiner[2], T. Burlingame[2]. [1]Kapi'olani Medical Center for Women and Children, Honolulu, Hawaii, and [2]Oregon Health Sciences University, Portland, Oregon.

Smith-Lemli-Opitz (SLO) syndrome is an autosomal recessive disorder which results from a defect in cholesterol biosynthesis. The finding of elevated levels of cholesterol precursors is diagnostic of SLO. There have been few reported cases of the prenatal diagnosis of SLO in the presence of a non-contributory family history. Abnormal triple screen, sex discrepancy, and polydactyly led to such a diagnosis in this case.

L.M. was a 29 year old G2 P1 AB0 who presented at 17.1 weeks gestation due to a positive maternal serum triple screen which estimated a midtrimester risk for fetal trisomy 18 of 1/15. The triple screen was reported as follows: MSAFP 0.44 MOM; ESTRIOL 0.43 MOM; HCG 0.35 MOM at 16.1 weeks. The couple opted for amniocentesis which resulted in a normal 46,XY karyotype. Due to a suspicion of early IUGR, a repeat ultrasound examination was performed at 20.1 weeks gestation, revealing a discrepancy between observed fetal sex and karyotype, post-axial polydactyly of both feet and the left hand, and growth lag. A repeat amniocentesis was performed to confirm fetal sex. L.M. was counseled regarding the sonographic and biochemical evidence that was suggestive of SLO. She elected to terminate the pregnancy. Amniotic fluid analysis subsequently revealed that 7-dehydrocholesterol (7-DHC) was greater than 800-fold increased in comparison to control; conversion of ergosterol to brassicasterol (estimating 7-DHC reductase activity) was 0.5% in fetal fibroblasts (control 15-35%, n=2), verifying SLO. Features consistent with SLO reported on autopsy included ambiguous genitalia with micropenis, severe hypospadias, and bifid scrotum. There was left hand post-axial polydactyly, bilateral post-axial polydactyly of the feet, and partial syndactyly of the second and third toes bilaterally. Facial dysmorphia included a broad nasal tip and anteverted nares, broad maxillary alveolar ridges, with a high arched hard palate and a soft palate cleft.

This case demonstrates a possible role for triple screen, particularly uE3 analysis, in the detection of fetuses at risk for SLO.