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Carrier screening in Gaucher disease: reproductive decision-making in couples with mixed heritage. V. Jansen, A. Starkman, L.Zajac, and R. Wallerstein. Human Genetics Program, Department of Pediatrics, New York University Medical Center, New York, N Y

Mutational analysis provides accurate assessment of Gaucher risk for reproductive decision-making in Eastern European Ashkenazi Jews as a small number of mutations account for most of the mutant alleles. More than 30% of the GD alleles correspond to a variety of rare mutations in other populations.

Carriers of known GD mutations who had a non-Jewish partner were ascertained through a screening program at New York University Medical Center. Each couple was recalled for counseling, results were reviewed and testing offered to the non-Jewish partner. Options included carrier testing by mutation analysis and/or enzymatic analysis and prenatal diagnosis.

We report the choices of the first twelve couples with a mixed heritage after learning that the Jewish partner was a Gaucher carrier. They included 3% of the total couples screened during the last year. Eleven of those couples were in a pregnancy; seven of the non-Jewish partners were male and five were female; five non-Jewish partners had both DNA and enzyme analysis; two chose enzyme analysis alone and another one had DNA screening only; finally, one couple had no additional testing; three couples elected prenatal Gaucher disease determination by amniocentesis with enzyme analysis; none of the non-Jewish partners were determined to be carriers; all of these pregnancies are ongoing but outcomes will be monitored for any affected infant. This study concludes that screening for Gaucher disease in couples with a mixed heritage is feasible. Guidelines for screening couples with mixed heritage need to be established. Both DNA and enzyme analysis should be performed on non-Jewish partners. Prenatal diagnosis should be offered for a definitive diagnosis.

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Kabuki make up syndrome in a Caribbean black child from Trinidad. M Jaquez MD, S. Wu MD, and E. Shirazi, BA. Dept. of Pediatrics, Univ. of Miami School of Medicine, FL.

The Kabuki make-up syndrome was first reported independently in 1981 by Niikawa and Kuroki. It is characterized by growth and mental retardation, dermatoglyphics abnormalities, and facial features resembling the stylized make-up worn by Kabuki actors. To date 100 cases have been reported, mostly of Japanese and Caucasian descent. Among these only two cases were of black ethnicity, one of which was mixed. We report the second case of Kabuki make-up syndrome in a non-mixed black male. He is a 5 ½ year old with growth deficiency in the first four years of life, which progressed to a low-normal percentile. He has moderate developmental delays, speech problems, some hyperactivity, mannerisms like hand flapping, cheerful behavior, out-toeing walk, stooped sitting posture with occasional drooling. He is on anticonvulsant medication for the past 6 months. Past medical history includes UTI, VUR, OME, diaphragmatic eventration, and submucose cleft palate. His craniofacial features show wide forehead and prominent occiput, long palpebral fissures, blue sclera, epicanthal folds, eyelid ectropion and ptosis of lower and upper eyelids respectively. Patient also presented with arching sparse eyebrows, short nasal septum, with depressed nasal tip, prominent filtrum, tented upper lip, and teeth abnormalities. The ears are prominent with bilateral tubes. Cardiothoracic abnormalities include pectus excavatum, I or II/ VI systolic murmur due to an ASD confirmed by echo. On chest x-ray the cardiac silhouette was mildly enlarged, right hemithorax smaller than left with mild shifting of the heart and mediastinum to the right. Patient also has right undescended and left retractile testes. The finger pads are very prominent with excess loops, broad first toe, and nail hypoplasia. Chromosomal analysis was normal.

Our patient, like the other reported black case, did not present with short stature at the age of 5 years. Therefore it may be possible that an ethnic factor accounts for such variations in height as comparison to other groups. To our knowledge, the mannerism and cheerful behavior of our patient, except for the mixed black case, has not been emphasized in other studies.

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Teaching Clinical Genetics to Pediatric Residents in an Outpatient Setting: A Proposed Model. M Jaquez MD, R Haun MD, R Frye MD, T Frazer, BA

The ambulatory care setting is one in which the pediatrician as a primary care provider excels in knowledge, skills, and effectiveness. He/she is particularly skilled in allaying the fears and concerns of parents as well as guiding them through complex care problems. Physician skills are heavily dependent on having a sufficient knowledge base in the various disciplines. In this new dawn of genetic medicine, our current methods of developing the resident's diagnostic and clinical management skills in genetics are not clearly defined. The fact that the half-life of the knowledge-base in applied clinical genetics is much shorter than in other fields provides an even greater challenge to the development of these teaching strategies. At this time, we have found very few programs with a well-developed model for teaching rudimentary diagnostic and management skills in clinical genetics for the pediatric resident-in-training. In any institution, the methods used to teach clinical genetic skills in a pediatric outpatient clinic must recognize the other teaching and service needs that are equally important to the program. We describe a protocol that is designed to develop the pediatric resident's skills and knowledge-base in clinical genetics while rotating through our outpatient clinics. There are two pathways whereby our residents develop their outpatient skills. In the morning clinics, three residents rotating in the Ambulatory Department are assigned to see faculty patients under their supervision, while in the afternoons, all the residents are assigned to their own patients in Continuity Care Clinic. The residents rotating on Ambulatory Care Service each month are assigned a specific case or topic in clinical genetics for which they will be responsible to develop the content of information sessions to the remainder of the resident staff at the beginning of their Continuity Care Clinic. Our intention is to develop a 36 month cycle of monthly topics with several of them repeated each year for the orientation of incoming house staff. An outpatient resource handbook in clinical genetics that the residents can refer to periodically will be developed from the monthly presentations and discussions and regularly updated.. A testing instrument will be developed to allow residents to periodically check their knowledge base against faculty's expectations. Further, a survey questionnaire will be developed and administered to the resident staff anonymously on a yearly basis to judge the effectiveness of the teaching program.

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RETROSPECTIVE ANALYSIS OF PATIENTS WITH OVERLAPPING FEATURES OF TOWNES-BROCKS SYNDROME AND GOLDENHAR SYNDROME. C.E. Keegan and B.R. Korf, Dept. of Medicine and Division of Genetics, Children's Hospital, Boston, MA

We conducted a retrospective chart analysis of seven patients with expanded spectrum hemifacial microsomia and imperforate anus to determine whether this subset of patients has undiagnosed Townes-Brocks syndrome. Townes-Brocks syndrome is characterized by the triad of imperforate anus, hand and foot anomalies, and ear anomalies. Hemifacial microsomia is not typically a feature of Townes-Brocks syndrome. Expanded spectrum hemifacial microsomia, or Goldenhar syndrome, consists of hemifacial microsomia, ear anomalies, vertebral anomalies, and eye anomalies, including epibulbar dermoids. Although imperforate anus has been reported in Goldenhar syndrome, it is not a common feature. Because these two syndromes have some overlapping features, it is often difficult to differentiate between these two entities in the clinical setting. However, Townes-Brocks syndrome is inherited in an autosomal dominant fashion, whereas Goldenhar is inherited sporadically, thereby emphasizing the importance of distinguishing between these two syndromes. We reviewed the medical records of six patients with expanded spectrum hemifacial microsomia for features of Townes-Brocks syndrome. Our results demonstrate that only one of these six patients could potentially be diagnosed as having Townes-Brocks syndrome. This patient has hemifacial microsomia, bilateral microtia, a left preaxial supernumerary thumb, a right epibulbar dermoid, and mild vertebral anomalies. She also has a tethered spinal cord and a hypoplastic right kidney. The other five patients had features more consistent with Goldenhar syndrome, VATER association, or other undefined syndromes. We are in the process of characterizing this subset of patients at a molecular level to more accurately predict their genetic risk. This will be done be sequencing the gene that is mutated in Townes-Brocks syndrome, the SALL1 transcription factor, in these patients.