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Autosomal recessive syndrome due to amazing consanguinity. Y. Lacassie, J. Avegno, A.H. Tilton. LSUHSC and Children's Hospital, New Orleans, Louisiana.

We report on a patient with a syndrome of MR/MCA who was the product of a highly consanguineous family. The patient was the result of a union between a man and his daughter. The daughter was in turn the product of a mating between the man and his mother. Major findings include: severe psychomotor and mental retardation, microcephaly with cerebral dysgenesis and cerebellar hypoplasia, delayed visual development, seizures, early hypotonia and late hypertonia; short stature and failure to thrive, early swallowing incoordination with aspiration pneumonias; dysmorphic face with striking hypertelorism, upslanting palpebral fissures and dysplastic, asymmetric, low-set ears; wide set nipples, sacral dimple, right inguinal hernia, hypospadias, cryptorchidism, overlapping fingers, and rocker-bottom feet. At onset of puberty, he developed severe scoliosis with secondary pulmonary restriction. He died at age 14 secondary to post-operative sepsis. Chromosomal and metabolic studies were normal. Although this patient presents some features of other syndromes (such as the Opitz-GBBB syndrome), the severity and peculiarity of his phenotype suggests a new, probably private, autosomal recessive disorder due to homozygosity for one or more loci.

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Ovarian Cancer Screening in Women from Hereditary Breast/Ovarian Cancer Families. S. Laframboise[1], R. Nedelcu[1], K.J. Murphy[1], D.E.C. Cole[2] and B. Rosen[1] [1]University of Toronto and Division of Gynecologic Oncology, Princess Margaret Hospital, Toronto, ON, Canada and [2] University of Toronto, Department of Biochemistry, Toronto, ON, Canada.

Women with a strong family history of ovarian and/or breast cancer may have an inherited predisposition to developing either or both of these cancers. The Familial Ovarian Cancer Clinic (FOCC), in a tertiary university setting, founded in 1992 has screened 1220 women to date; 269 women deemed *high-risk* based on their family history are the subject of this study. The objectives of the study were as follows: 1) to determine the effectiveness of routine screening using CA-125 and pelvic/trans-vaginal ultrasound to detect early cancer, 2) to establish the cost-effectiveness of the program, 3) to provide guidelines for similar screening programs. All women have been seen in the clinic at least once, and as many as 16 visits. Overall, 2.9% (31/1051) of the CA-125 results were abnormal, or greater than 35 U/ml; 17% (198/1162) ultrasounds were abnormal, with abnormalities ranging from benign appearing cystic changes to more ominous findings. Nineteen (7%) women with known BRCA1/2 mutations underwent surgery; in 11 women, the pre-operative US was abnormal. All pre-operative CA-125 blood tests were normal. Overall, 1 (0.4%) woman was diagnosed with ovarian cancer, a stage IA, grade 1 endometrioid adenocarcinoma. Screening tools are imperfect. CA-125 lacks sensitivity, while US's specificity is low (56%). Therefore, the routine use of these tests in women "at risk" (low or medium) is questionable. Certainly, in women properly assessed as being high risk, at present time, no better screening schema has been proven. Therefore, the routine use of CA-125 and US for women "at risk" should be reserved to women participating in an organized screening program. For those women at a lower risk based on family history, the merits of screening are questionable.

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A BRCA1 mutation carrier with three breast primaries and childhood ionizing radiation treatments: A possible gene/environment interaction. P.J. Levonian, M.S. Williams. Gundersen Lutheran Medical Center, La Crosse, WI.

We report here on a 37-year-old BRCA1 mutation carrier female who has had multiple primary breast cancers and a childhood history of radiation therapy. In 1962, this patient presented at 6 months of age with a palpable abdominal mass which was found to be an infantile hemangio-endothelioma. She received seven radiation treatments for this condition. The radiation field in this six-month-old female was a medial ventral field which extended to just above the lower margin of the rib cage. She had no recurrence of her liver lesion. At the age of 25, she was diagnosed with an infiltrating medullary carcinoma of the right breast. She was treated with lumpectomy and radiation therapy. At age 30, she was diagnosed with an infiltrating ductal carcinoma of the left breast. At age 31, she was diagnosed with her third primary, an infiltrating ductal carcinoma of the right breast. At age 37, she was found to carry a deleterious mutation in the BRCA1 gene (3171ins5). Although her 57-year-old mother was recently diagnosed with breast cancer, the BRCA1 mutation was found to be paternally inherited. The 3171ins5 mutation has been previously shown to be a disease-causing mutation in other families. Undoubtedly, this patient's history of three primary breast carcinomas is explained by the presence of this deleterious mutation. However, the presentation in this patient is strikingly early and severe. We speculate that this patient's early childhood radiation treatments may have played an environmental role in carcinogenesis in this patient. The orthovoltage machines used at that time may have allowed for substantial radiation scatter in a six-month-old. It is possible that the breast tissue may have received ionizing radiation which produced a "second hit" in the maternally inherited wild-type BRCA1 gene. Individuals with BRCA1 gene mutations are felt to be at moderately increased risk for developing colon cancer. We speculate that this patient may be at substantially increased risk because of the inevitable high radiation doses received by her colon in the early childhood period. We present this as a possible example of gene/environment interaction.

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Ruvalcaba Syndrome (a rare progeroid syndrome). A new case and review of the literature.

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In 1971, Ruvalcaba et. al. described a familial multiple congenital anomaly syndrome characterized by skeletal dysplasia, short stature, small hands and feet, microcephaly, unusual face, and mental retardation. Similar cases previously reported by Hunter (1977/six cases) were reclassified as Hunter Mc. Alpine, and those from Sugio and Kajii (1984/ five cases), as tricho-rhino-phalangeal syndrome type III.

We report a 14 year-old female with skeletal dysplasia, peculiar facies (progeroid), mental retardation, microcephaly, sparse hair, high forehead, arched eyebrows, downslanting palpebral fissures, puberal delay, beaked nose with hypoplastic nasal alae, microstomia with narrow maxilla, thin lips, downturned mouth corners, large areolae, hypoplasytic skin, pectus excavatum, joint limitations, small hands with short phalangs and metacapals and coned epiphyses, short fingers and toes. In addition, she had several anomalies not previously described such as severe congenital cardiac malformation, bilateral coroidosis. By analyzing groups of similar patients, either familial or sporadic, it may be possible to define the diagnostic clinical criteria for this syndrome, and also outline the variability of the manifestations and its natural history. The cause of Ruvalcaba syndrome remains unclear. The occurrence of the syndrome suggests autosomal dominance inheritance with incomplete penetrance. The relevance of this paper is the new clinical findings revealed by our patient and that in addition it represents the 8th case reported in the literature, and the first in Venezuela.