111

NEONATAL OUTCOMES AND THE USE OF GLYBURIDE IN GESTATIONAL DIABETES MELLITUS. R.M. Reynolds. B.F. Kahn, J.K. Davies, A.M. Lynch, L.A. Barbour, Departments of Pediatrics, Obstetrics and Gynecology, Biometrics and Preventive Medicine, and Medicine, University of Colorado Health Sciences Center, Denver, CO.

Background: The prevalence of gestational diabetes mellitus (GDM) continues to rise in the face of the obesity epidemic affecting up to 14% of some ethnic populations. Studies have shown that treatment of GDM with insulin decreases serious maternal and fetal morbidity and perinatal mortality. Oral medications are preferred by patients and this could lead to increased compliance. Glyburide remains unapproved for use in GDM. Study: This was a retrospective review of 124 women who were offered glyburide therapy between November 2000 and May 2005. A cohort of 101 women was included for analysis, approximately 50% Hispanic, 33% Caucasian, and 3% African American. Neonatal outcomes reviewed included birth weight, macrosomia, weight > 90%, admission to the neonatal intensive care unit, hypoglycemia, evidence of respiratory distress (RDS), and congenital anomalies. Results: Eighty percent of the pregnancies were treated successfully with glyburide. There were no reported perinatal deaths. Overall cesarean section rate was 27% and there were no reports of shoulder dystocia. The macrosomia rate was 7% and 27% of the infants were large for gestational age (IGA) with a mean birth weight of 3,307 ± 490 g. Although 21% were admitted to the NICU, only 8% required IV glucose for hypoglycemia and only 8% were treated for RDS. Three congenital anomalies were noted but glyburide was initiated after 22 weeks gestation. Conclusion: Although the study was a retrospective retrieval of data, the management of these patients was standardized. Fetal growth was considered in the decisions regarding titration of glyburide and this may have contributed to neonatal outcomes such as weight, shoulder dystocia, and rate of cesarean section. Given that the relative safety of glyburide has been confirmed, outcomes with glyburide are at least comparable to outcomes with insulin, and oral medications are preferred to insulin and this may increase compliance, glyburide would be another option to treat GDM and therefore improve overall fetal morbidi

112

GEOGRAPHIC AND OCCUPATIONAL RISK FACTORS FOR VENTRICULAR SEPTAL

DEFECTS, WASHINGTON STATE 1987–2003. M. Batra, ^{1,2} C.L. Heike, ^{1,2} R.C. Phillips, ^{2,3} N.S. Weiss, ² ¹Pediatrics, University of Washington and Children's Hospital and Regional Medical Center, Seattle, WA, ²Epidemiology, School of Public Health and Community Medicine, University of Washington, Seattle, WA, ³Medical Education and Health Informatics, University of Washington, Seattle, WA.

Purpose of Study: To address the hypothesis that parents' environmental and occupational exposures can influence the presence of a ventricular septal defect (VSD) in their offspring, we conducted a population-based case-control study of infants born in Washington State from 1987–2003. Methods: We used birth certificate data linked with hospital discharge information to identify children diagnosed with VSD within the first 2 years of life (N = 13,290). From the birth certificate data, we obtained information on parental occupation and county of maternal residence. The latter was categorized according to region (east-west), rural-urban classification, and proportion of farm land and rop land. Results: Risk of VSD was greater for infants whose mothers resided neastern Washington (odds ratio 1.30, 95% confidence interval: 1.03, 1.65). VSD in conjunction with other cardiac malformations (n = 1,205) exhibited a stronger geographical association than isolated VSD (n = 2,284). Analyses restricted to eastern Washington did not reveal a clear relationship between risk of VSD and increasing proportion of agricultural land in the mother's county of residence. Parental occupation in agriculture was not associated with the presence of VSD. Conclusions: While these findings suggest regional variation in Washington State in the occurrence of VSD, the basis for this variation remains to be determined.

The first author is supported by UW NIH K30 Program and is a fellow in training.

113

NEONATOLOGY WITHOUT INDOMETHACIN OR BOWEL PERFORATION: A 19-YEAR EXPERIENCE. I. Pietz, P. Achanti, E.C. Stepka, S. Mehta, Fairview Hospital, Cleveland,

Objective: Review the use of indomethacin and a strict feeding protocol for VLBW. Methods: Review the incidence of NEC, IVH, and bowel perforation as our policies for using Indocin and a strict feeding protocol changed. From 1986–1991, 0/228 VLBW babies had NEC. 0/228 had bowel perforation. From 1991–2001, 0/683 VLBW babies had bowel perforation. Before 2001, our feeding protocol advanced only 4 mL/kg/day for VLBW babies. In 2001, the protocol was liberalized and Indocin use was allowed. In April of 2003, after 2 cases of NEC, we reverted to the original feeding protocol and stopped using Indocin. For 2001–2004 we compare 261 VLBW babies to the Vermont-Oxford network. 10/149 infants received indomethacin in 2001–2002. 0/112 infants received indomethacin in 2003–2004. Two infants had NEC (2/261). The first received Indocin and was on liberal feedings. The second had no Indocin but was on liberal feedings. Both recovered without surgery. Rates of NEC, bowel perforation, IVH, and CLD are shown below. Comparisons to 2003 Vermont-Oxford data are shown below. Our incidence of IVH, SIVH, NEC, bowel perforation, and BPD was lower than network. Studies show prophylactic Indocin is associated with reduced incidence of IVH. In Bandstra's study the early Indocin group had incidence of IVH greater than ours (23% vs 11%). In Ment's study an early Indocin group had an incidence (12% vs 11%) similar to ours. In the last 30 months, we have not used Indocin and we adhere to our feeding protocol. Our NEC rate is again 0%; our bowel perforation rate from 1986–2004 = 0/1172. Our IVH and BPD rates are also low. Conclusion: In this NICU using our feeding protocol without Indocin is advisable.

		April	
1986-2001	3041-2002		94/2003 to 12/2004
No Indocis State Feeding Protectal State (Pro) Bened Perforation 6/201 (PS) (YE 20228 (PS)	3001 - 5002 Indexis (18/149) Liberal Forders Protects NEC 2049 (13/1) Breat Parlieration 8149 (8/4) 173 15149 (13/4) Grade IV 2149 (13/4) Classics (12/4)	-	No Inducto State Feeding Posterol State Feeding Posterol State State (PN) Based Posterolina 8112 (PN) INH ISA12 (INN) INH ISA12 (INN) INH IN 4112 (IAN) (IA) 1112 (IAN)

	Expected Vermont-Oxford	Actual 2003-2004 N=112
NEC	(6%)	(.89%)
Bowel Perforation	(2%)	(0%)
IVH	(26%)	(13%)
SIVH	(6%)	(3.4%)
BPD	(29%)	(16%)

Genetics Concurrent Session 8:30 AM

Friday, February 3, 2006

114

A CASE OF AUTOSOMAL RECESSIVE INFANTILE OSTEOPETROSIS DUE TO MUTATION IN TCIRGI PRESENTING WITH MULTIPLE CONGENITAL ANOMALIES. R. Conway, R.

Lachman, C. Hurvitz, R. Falk, Cedars-Sinai Medical Center, Los Angeles, CA.
Autosomal recessive infantile osteopetrosis (ARIO) is a rare and potentially fatal disorder of bone metabolism caused by a defect in osteoclast function. The pathologic features are secondary to insufficient bone resorption and usually present in the infancy. Symptoms include sclerotic bones leading to bone marrow compromise with resultant pancytopenia, cranial nerve impingement, hydrocephalus, and fracture. This is an autosomal recessive disorder caused by mutations in either TCIRG1, CLCN7, or OSTM1. Malformations are not a part of this disorder. We present a 6-month-old male, the first child between nonconsanguineous parents, who was referred to our clinic for limb defects. Findings prompting the referral included congenital left upper limb anomalies of syndactyly and radial-ulnar synostosis. There was an ipsilateral anterior rib defect, though there was no clinically appreciable hypoplasia of the pectoralis major. He also had a left low-lying, cross-fused kidney. Besides the limb anomalies, the patient presented in our clinic having signs of hydrocephalus. He had left facial nerve palsy and oculomotor abnormalities. The diagnosis of ARIO was made after hospitalization; radiographs demonstrated characteristic findings of diffuse osteosclerosis and periosteal thickening in all bones. The patient had surgical management for noncommunicating hydrocephalus with good results. The majority of cases with ARIO are compound heterozygotes. Reported homozygous patients most commonly result from a consanguineous mating or come from an isolated population (Costa Rica). Genetic testing of this patient revealed homozygosity for a rare mutation in TCIRG1, a subunit of the osteoclast vacuolar proton pump. Because this child was a product of a non-consanguineous union, this was an unexpected result. To explain the malformations in this case, we postulated either uniparental disomy or a spontaneous contiguous gene deletion on one chromosome that included the *TCIRG1* gene, which then unmasked a hemizygous recessive state. Subsequent sequence analysis of both parents for *TCIRG1* mutations showed that each was a heterozygous carrier of their son's mutation. The presence of the limb and kidney anomalies complicated the diagnosis in this case. No other reported patients with ARIO have had similar birth defects. Without treatment, early demise secondary to bone marrow failure is predicted in nearly all cases. Associated features, natural history, and management recommendations for ARIO will be reviewed.

115

AN INFANT WITH CONDUCTIVE DEAFNESS, ONYCHODYSTROPHY, OSTEODYSTROPHY, DEVELOPMENTAL DELAY, AND DYSMORPHISM: IS THIS DOOR SYNDROME? M.M. Martin, A.M. Slavotinek, Department of Pediatrics, Division of

Genetics, University of California, San Francisco, San Francisco, CA.

Introduction: DOOR syndrome was an acronym first suggested by Cantwell in 1975 to describe a constellation of findings including deafness, onychodystrophy, osteodystrophy, and retardation. It is a genetically heterogeneous condition with both autosomal recessive and dominant forms. The deafness and onychodystrophy are common to both forms, but mental retardation is a feature of the recessive form. A number of patients with the recessive form have had elevated 2-oxoglutarate levels in plasma and urine and one study showed a correlation between the elevated levels and decreased activity of the 2-oxoglutarate decarboxylase enzyme (E10). It has been suggested that elevation of this compound may be associated with a more severe, and even lethal, phenotype. We present a patient who possesses the cardinal features of DOOR syndrome but who has additional dysmorphic features. **Case:** The baby was born at 36 weeks' gestation to a 32-year-old G4 P2–3 female. Birth weight and length were both < 10th centile. Work-up for a congenital infection was negative. Relevant findings were an ASD and VSD at 1 month of age and conductive hearing loss at 2 months. At 3 months of age, growth parameters were all less than the 3rd centile. Her exam showed brachycephaly, a large fontanel, narrow and upslanting palpebral fissures, a bulbous nasal tip with anteverted nares, a smooth philtrum, thin upper lip, brachydactyly, hypoplastic thumbs, and hypoplastic finger and toenails. She was developmentally delayed with poor head control. Chromosome analysis showed a normal female karyotype and urine organic acids were normal with no elevation of 2-oxoglutarate. A skeletal survey in the newborn period showed absent and hypoplastic ossification centers of the fingers and toes. Family history was noncontributory. **Conclusion:** The diagnosis of DOOR syndrome is based on clinical examination as the pathogenesis is unknown and there is no cytogenetic or molecular testing. We consider that our patient has DOOR syndrome because of onychodystrophy, delayed ossification of the phalanges, deafness, and developmental delay. In addition, there have been reports of congenital anomalies including septal heart defects. However, the dysmorphism in our patient is not typical of this condition and is unexplained. Conductive hearing loss is also less frequent than sensorineural hearing loss in DOOR syndrome. We believe that our patient may represent a less severe presentation of the autosomal recessive form of DOOR syndrome.

116

A LETHAL SKELETAL DYSPLASIA RESEMBLING DESBUQUOIS DYSPLASIA.

V.K. Agarwal, K. Bui, D. Salazar, R.S. Lachman, D.R. Witt, F. Field, D.L. Rimoin, W.R. Wilcox, Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, CA. Desbuquois dysplasia is a rare form of short limb dwarfism with autosomal recessive inheritance characterized by severe short stature of prenatal onset, joint laxity, facial dysmorphic features, spur-like projections of the proximal femora ("Swedish key" or "monkey wrench"), mild vertebral and epiphyseal abnormalities, and advanced carpal and tarsal bone age. Cases may be divided into two groups depending on whether or not typical hand abnormalities are present, which include an extra ossification center distal to the second metacarpal and/or a delta phalanx of the thumb. A recent genome-wide search in four inbred Desbuquois families with typical hand abnormalities demonstrated linkage to chromosome 17q25.3. Exclusion of the 17q25.3 locus in the clinical subtype of Desbuquois dys

plasia without typical hand anomalies in three inbred families was subsequently reported. We report a new family of at least four siblings and one first cousin affected with a lethal Desbuquois-like dysplasia with typical hand abnormalities. Further genomic analysis excludes linkage to chromosome 17q25.3 in this family.

117

SPLIT HAND-SPLIT FOOT MALFORMATION 3 AT 10Q24: CLINICAL AND LABORATORY DIAGNOSIS AND GENE SEARCH. C.D. DeLozier, 1,2 R. Lyle,2 U. Radhakrishna,

C. Schwartz, S.E. Antonarakis, I.L. Blouin, Genetic Medicine Central California and UCSF-Fresno; ²Department of Genetic Medicine and Development, University of Geneva, Switzerland; 3JC Self Research Institute, Greenwood Genetics Center, Greenwood, SC. Split hand/split foot disorder (SHFM, also called ectrodactyly) is a clinically and genetically heterogeneous group of congenital limb malformations, which includes syndromic and nonsyndromic forms. The typical limb defect is a deep median cleft due to absence of the central rays, affecting from one to all four members, with feet more often and more significantly affected than hands. SHFM can, however, present with a range of malformations of highly variable severity even within a family. The inheritance pattern in most families is autosomal dominant, with variable penetrance. However, autosomal recessive and X-linked forms have also been described. Five SHFM loci have been mapped: SHFM1 (7q21), SHFM2 (Xq26), SHFM3 (10q24), SHFM4 (3q27), and SHFM5 (2q31). To date mutations in a specific gene (TP63) have been identified only for SHFM4. We have studied three large families with SHFM3, showing the classical autosomal dominant transmission and variable severity. After first mapping these families to 10q24, we have worked on defining the mechanism of gene disruption, which can be shown by pulsed-field gel electrophoresis to be caused by an approximately 500 kb DNA rearrangement. This region contains a number of candidate genes for SHFM3, but the gene or genes involved in the pathogenesis of SHFM3 are not yet known. We have developed a diagnostic test for SHFM3 that uses two different techniques, FISH and quantitative PCR, to show that SHFM3 is caused by a minimal 325 kb duplication containing only two genes (BTRC and POLL). The data presented provide improved methods for diagnosis and begin to elucidate the pathogenic mechanism of SHFM3, as at least 2 genes of 13 studied from the 10q24 region are overexpressed in SHFM3 patients as compared to controls.

118

INTRACELLULAR GLUTATHIONE LEVELS ARE LOW IN PERIPHERAL BLOOD CELLS IN PATIENTS WITH PRIMARY OR SECONDARY MITOCHONDRIAL DYSFUNCTION. K.R. Atkuri, ¹ L.A. Herzenberg, ¹ G.M. Enns, ² Department of Genetics and ²Department of

Pediatrics, Division of Medical Genetics, Stanford University, Stanford, CA.

Introduction: Both primary and secondary mitochondrial respiratory chain dysfunction result in generation of abnormal levels of free radicals that deplete intracellular stores of glutathione. The glutathione system is the main natural defense mechanism that helps to combat oxidative damage. We report the intracellular reduced glutathione (iGSH) levels in patients with either primary mitochondrial disease or organic acidemias. Methods: Thirtyfive subjects, classified as having either known electron transport chain defects (eg, specific complex deficiencies, pathogenic mtDNA mutations) (n = 17), unknown mitochondrial disease (n = 9), or organic acidemias (n = 9) were studied. Peripheral blood buffy coats were treated with monochlorobimane (MCB), then stained for leukocyte subset markers and subjected to Hi-D fluorescence activated cell sorting (FACS). **Results:** *Primary mitochon*drial disorders: When compared to normal controls (n=20), iGSH levels in CD4 T cells (MCB ratio 1.38 ± 0.32 v. 1.66 ± 0.27 in controls, p=.004), CD8 T cells (MCB ratio 1.29 ± 0.29 v. 1.52 ± 0.21 in controls, p=.001), B cells (MCB ratio 0.65 ± 0.2 v 0.98 ± 0.2 in controls, p = .03), and monocytes (MCB ratio 0.96 \pm 0.18 v 1.25 \pm 0.2 in controls, p = .04) were significantly lower in mitochondrial disease subjects who were not on antioxidants. No significant difference in either T cell subtype was seen in those taking antioxidants when compared to normal controls. iGSH levels in neutrophils tended to be lower in patients that were not on antioxidants (*p* = .057). *Organic acidemias*: When compared to normal controls (n = 20), iGSH levels in CD4 T cells (MCB ratio 1.12 \pm 0.15 v. 1.69 \pm 0.27 in controls, p = .002), CD8 T cells (MCB ratio 1.04 ± 0.20 v. 1.52 ± 0.21 in controls, p = .003), neutrophils (MCB ratio 0.69 ± 0.24 v. 1.00 ± 0.24 , p = .044), and monocytes (MCB ratio 0.90 ± 0.28 v 1.22 ± 0.24 v. 1.00 ± 0.24 v. 1.0.25, p = .045) were significantly lower in subjects with organic acidemias. No significant difference in iGSH levels was observed in B cells. **Conclusions:** T cells (CD4 and CD8 subsets), neutrophils, and monocytes may have lower iGSH levels in mitochondrial disorders and organic acidemias. In subjects taking antioxidants, there appears to be sparing of iGSH levels. The significance of the selective low iGSH levels in T cell subsets when compared to B cells is unclear. Given that T cell iGSH levels tend to be low in mitochondrial disorders and organic acidemias, it is reasonable to explore the therapeutic effect of N-acetylcysteine in these disorders.

119

MUTATIONAL ANALYSIS OF PATIENTS WITH NONKETOTIC HYPERGLYCINEMIA AND THE IDENTIFICATION OF LARGE DELETIONS IN THE GLDC GENE USING A NOVEL **DETECTION SYSTEM.** L.N. Puls, G. Scharer, J.L. Van Hove, University of Colorado Health

Sciences Center, Aurora, CO.

Nonketotic hyperglycinemia (NKH) is an autosomal recessive disorder of glycine metabolism caused by a defect in the glycine cleavage system and characterized by neurological disease. Severity of presentation varies considerably and, to date, prognosis is entirely based on extent of symptoms. We present a molecular study of 35 patients diagnosed with NKH. Mutations in either the glycine decarboxylase (GLDC) or the aminotransferase (AMT) protein of the cleavage system were identified in all 35 patients, many of which were novel mutations. We propose here that prognostic outcome in NKH patients is rooted in the nature of the mutations in two key genes. Through molecular analysis of the AMT and GLDCgenes in both patients and parents, we can utilize genotypic information to help predict severity of outcome. In concordance with this goal, we have also designed a method of deletion detection for exon 3 of GLDC. Deletions encompassing in this exon have been identified in many NKH patients. However, compound heterozygosity precludes these deletions from detection by direct sequencing. Our detection system is based on real-time, quantitative PCR and utilizes the pseudogene to GLDC as an internal control. This technical control is the pseudogene to GLDC as an internal control. nique has allowed identification of 8 individuals possessing a large deletion in GLDC. Pedigree and Southern blot analysis verify these results. An increased ability to detect mutation and predict phenotype will aid in identifying patients who would benefit from available treatment. Since decisions to abort or continue pregnancy may depend on predicted severity, molecular analysis will greatly aid in prenatal testing options as well.

DNA HYPOMETHYLATION AND NEURONAL SURVIVAL. A. Thaker, L. Hutnick, G. Fan, Department of Human Genetics, UCLA, Los Angeles, CA. DNA cytosine methylation in vertebrate animals is a major epigenetic modification

involved in gene regulation, genomic imprinting, and X-inactivation during development. To understand the role of DNA methylation in CNS development, specific conditional knockout mice for the maintenance enzyme DNA methyltransferase I (Dnmt1) were previously generated using the cre/loxP system. Linking cre recombinase to the Emx-1 promoter restricted the deletion to pallial cortical precursors that give rise to the neocortex and hippocampus. Cre/LoxP-mediated Dnmt1 deletion occurred in precursor cells between E9–12, resulting in hypomethylated postmitotic cortical and hippocampal neurons during midgestation. Massive neuronal degeneration was evident upon gross observation with a dramatic reduction of cortical and hippocampal structures. TUNEL staining suggests that hypomethylated cortical neurons and precursor cells undergo apoptotic cell death at around E14. It has also been previously reported that Dnmt1 deletion in primary fibroblasts results in cell death via a p53-mediated pathway. This study sought to investigate if a similar, p53-dependent mechanism is involved in the cortical and hippocampal cell death observed in the aforementioned Dnmt1 conditional knockouts. Western blot analysis failed to show induction of an active, serine-phosphorylated (S15) form of p53 in E15 mutant cell lysate. However, preliminary data from quantitative, real-time PCR reveal that there is an induction of p53 transcript and its downstream product p21 in mutant cDNA at E13.5. Additional investigation is required to determine which active, phosphorylated form of p53 is up-regulated in Dnmt1-deficient apoptotic neurons and which additional downstream targets of p53 are involved.

121

DISCORDANT MONOZYGOTIC TWINS WITH WILDERVANCK SYNDROME: A PROPOSED MODE OF INHERITANCE. N. Vatanavicharn, 1 J.M. Graham Jr, 1 K. Dawson, 1 J. Kohlase,² Department of Pediatrics/Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, CA; ²Institute of Human Genetics and Anthropology, Freiburg University, Germany.

Wildervanck syndrome or cervico-oculo-acoustic syndrome is a recognizable malformation syndrome with major clinical features including Klippel-Feil sequence, Duane retraction syndrome, hypoplastic thumbs, and sensorineural hearing loss. Affected individuals with these findings must be differentiated from other malformation syndromes, including Townes-Brocks syndrome, Okihiro syndrome, Goldenhar syndrome, and MURCS association. Most previous reported cases with Wildervanck syndrome have been sporadic and female, although a few males with the condition have been described. Several modes of inheritance have been proposed, but X-linked inheritance appears most likely. We report an 18-year-old female with Wildervanck syndrome and her unaffected monozygous twin sister. She was the product of a twin pregnancy. She and her twin sister were born to her 23-year-old G1 mother and 25-year-old father after an uncomplicated pregnancy. The neonatal course was uneventful. She was previously diagnosed with Goldenhar syndrome based on the clinical features of a right epibulbar dermoid, small and dysplastic ears with bilateral preauricular tags, mild facial hypoplasia of the right, butterfly vertebrae. She has profound sensorineural hearing loss on the right and mild-moderate mixed hearing loss on the left. She has poor vision on the right, but left eyesight is normal. Development of gross motor skills was normal, although she had difficulty with balance. Her speech was delayed. Skeletal anomalies include hypoplastic thumbs with ankylosis, progressive scoliosis, congenital fusion in the lower cervical spine C5 and C6, and butterfly vertebrae in the upper thoracic spine. She also has Duane retraction syndrome. She had been clinically diagnosed with Okihiro syndrome, but complete SAL14 gene sequencing was not able to identify a mutation, and molecular analysis confirmed monozygousity. We propose that this female has Wildervanck syndrome with unaffected identical twin sister. Skewed X inactivation might explain discordance in the monozygotic twins, suggesting X-linked dominant inheritance. Review of the literature on Okihiro syndrome and Wildervanck syndrome will be

122

EXPANDING THE PHENOTYPE OF MOSAIC TRISOMY 20. M.J.H. Willis, 1 L.M. Bird, 1,3

M. Dell'Aquilla, ^{1,2} M.C. Jones, ^{1,3} 'Department of Pediatrics, ²Department of Medicine, University of California, San Diego; ³Children's Hospital San Diego. Mosaic trisomy 20 is one of the more common cytogenetic abnormalities found on amnio-

centesis or chorionic villus sampling. Studies have shown that outcome is normal in 90-93% of prenatally diagnosed cases. There are, however, reports in the literature of children with mosaic trisomy 20 described as having an assortment of dysmorphic features and varying levels of developmental delay. Unfortunately, the literature has not defined a specific phenotype for this entity. Here we report three patients diagnosed prenatally with mosaic trisomy 20. Over a number of years of follow-up it has become apparent that there are some striking similarities among the three. Comparison between our patients and the literature cases suggests a more consistent phenotype than has previously been suggested. Recurring features include spinal abnormalities (including spinal stenosis, vertebral fusion, and kyphosis), hypotonia, lifelong constipation and possible colonic agangliosis, sloped shoulders, and significant learning disabilities despite normal intelligence. These findings may be overlooked on routine history and physical exam or assumed to be standard pediatric problems. It is not our intention to suggest that there is a distinctive face for this entity but to suggest that a subtle phenotype does exist. We have attempted to identify a set of findings for which any child diagnosed with mosaic trisomy 20 should be assessed or followed even in the presence of an apparently normal physical exam at birth.