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SPONDYLOEPIPHYSEAL DYSPLASIA, CONGENITA
NATURAL HISTORY

INTRODUCTION:

The following summary of the medical expectations in Spondyloepiphyseal Dysplasia, Congenita (SEDC) is neither exhaustive nor cited. It is based upon the available literature as well as personal experience in the Midwest Regional Bone Dysplasia Clinics (MRBDC). It is meant to provide a guideline for the kinds of problems that may arise in children with this disorder, and particularly to help clinicians caring for a recently diagnosed child. For specific questions or more detailed discussions, feel free to contact MRBDC at the University of Wisconsin – Madison [phone – 608 262 6228; fax – 608 263 3496; email – modaff@waisman.wisc.edu].

Spondyloepiphyseal dysplasia is a non-specific diagnostic designation that simply describes the primary radiologic manifestations seen – spine abnormalities ('spondylo') and abnormalities of the epiphyses. There a number of forms of spondyloepiphyseal dysplasia as well as substantial numbers of individuals who don't seem to correspond to any specific form that has been previously described and delineated. SEDC is the most common spondyloepiphyseal dysplasia and the most common 'short trunk' dwarfing bone dysplasia. Individuals will typically have both a short trunk and a constricted chest from birth and arms and legs that appear to be disproportionately long. Radiographs show rounded and flattened vertebral bodies and marked delay in appearance of the epiphyses (so that, for example, the femoral heads may not appear at all ossified until mid-childhood or early adolescence).

MEDICAL ISSUES AND PARENTAL CONCERNS TO BE ANTICIPATED

PROBLEM: **GROWTH**
EXPECTATIONS: Marked short stature is to be expected; ultimate adult height is usually between 3 feet and 4 feet.
MONITORING: Monitor growth using (the rather rudimentary) SEDC-specific growth grid.
INTERVENTION: There is no known treatment. Growth hormone is not likely to be effective since this disorder is secondary to intrinsic abnormality of bone growth. Limb lengthening, suggested but controversial in other short stature syndromes, is probably not an option since much of the effects of this disorder is on spine growth not just the limbs. Therefore one can anticipate even

more disproportion if the limbs are lengthened. Limb lengthening may also negatively affect already intrinsically abnormal joints.

PROBLEM: **DEVELOPMENT**
EXPECTATIONS: Intelligence is normal unless complications intervene. Variations in developmental patterns and particularly gross motor delays are to be expected because of the marked short stature.
MONITORING: Routine.
INTERVENTION: None.

PROBLEM: **NEUROLOGIC COMPLICATIONS**
EXPECTATIONS: There is considerable risk associated with frequent instability of the cervical spine, which, if present, can result in upper cervical cord compression [chronically or acutely] and consequent paralysis or related problems. Even if an apparently stable cervical spine is first identified, risk remains that instability may develop later.
MONITORING: Watch for signs of upper cervical myelopathy including lethargy, failure to thrive, marked hypotonia, decreased motor endurance, long track signs [asymmetric strength, asymmetric or increased deep tendon reflexes, sensory changes]. Lateral cervical spine films [flexion, neutral and extension] should be obtained in the first 6 months of life; if abnormal or equivocal, repeat as part of complete assessment every 6 months. Neurologic examination should be completed every 6-12 months if there is no apparent instability on x-rays or every 3 months if instability is present.
INTERVENTION: If instability is present, limit neck movement and uncontrolled head movement including no forced flexion with diaper changing, no swingomatic use, use of rear-facing car seat for as long as feasible. If instability is severe, cervical spine fusion is needed. When needed, this probably should be done before independent walking. There has been a high failure rate of fusions and consultation with specialists with experience in performing cervical spine fusion in children with SEDC should be sought.

PROBLEM: **MACROCEPHALY**
EXPECTATIONS: Some children have experienced acceleration of head growth in the first two years of life. This is secondary to benign extraaxial fluid accumulation.
MONITORING: If acceleration occurs, will need neuroimaging.
INTERVENTION: If imaging shows extraaxial fluid accumulation, then no treatment is indicated.

PROBLEM: **SPINE**
EXPECTATIONS: There is high risk for early onset kyphoscoliosis. Many also have marked hyperlordosis (in part driven by abnormalities of the hips) that may cause chronic, recurrent low back pain.
MONITORING: Clinical examination for development of kyphoscoliosis every 6 months. AP and lateral spine x-rays if there is any clinical indication of curve developing. If pain arises associated with hyperlordosis, physical therapy for lower abdominal muscle strengthening and

pelvic rotation exercises may be of some benefit.
INTERVENTION: Scoliosis frequently will require bracing in childhood and often will require surgical fusion.

PROBLEM: **CLEFT PALATE**
EXPECTATIONS: Large minority of individuals with SEDC will have frank or submucosal clefts.
MONITORING: If present, child is at greater risk for middle ear disease and hearing loss [see below].
INTERVENTION: If present, repair using the usual age and weight criteria.

PROBLEM: **HEARING LOSS**
EXPECTATIONS: Although usually middle ear disease related, some have a more significant sensorineural component. Even if no hearing loss is initially demonstrated, some individuals will develop a mixed and progressive loss at some time in childhood.
MONITORING: Audiometric testing at 12, 18 and 24 months and once yearly thereafter.
INTERVENTION: Episodes of acute or serous otitis should be aggressively treated and myringotomy and tube placement should be used liberally for recurrent or persistent problems. Amplification may be needed if mixed loss is more than very mild.

PROBLEM: **EYE PROBLEMS**
EXPECTATIONS: High myopia is very common. There is moderate to marked risk for retinal detachments in those with high myopia. In those in whom marked myopia is not present, the risk for retinal detachment is much lower but not zero.
MONITORING: Ophthalmologic assessment within the first 6 months of life and then every 6-12 months. Immediate reevaluation for any recognized change in vision or other indicators of possible retinal detachment. The affected child and the child's parents should be taught the signs and symptoms of retinal detachment.
INTERVENTION: Early surgery for retinal detachment can be vision-saving.

PROBLEM: **HIPS**
EXPECTATIONS: Coxa vara is usual. Sometimes severe pain arises. Virtually all have premature hip degeneration in young adulthood.
MONITORING: Radiologic assessment at around 4 y of age, or sooner if serious hip abnormality is suspected. One can anticipate that femoral head ossification will not occur until later childhood.
INTERVENTION: The aim is to have stable, pain free, functional hips. Surgical realignment (femoral valgus and extension osteotomies) is indicated <u>if</u> intractable pain or marked limits of mobility are present. Even in the absence of these indicators, realignment may make total hip replacement easier later. Limitations of repetitive weight bearing activities can slow degenerative arthritic changes. Hip replacement is often needed in the 30s or 40s.

PROBLEM: **FEET**
EXPECTATIONS: Occasionally will have clubfoot deformity.
MONITORING: Assess in infancy.
INTERVENTION: Not particularly resistant to usual orthopedic therapy.

PROBLEM: **RESPIRATORY**
EXPECTATIONS: Two problems, alone or in combination, may be present and may be potentially life-threatening: a. laryngotracheobronchomalacia; b. chest constriction. They can result in risk for chronic hypoxia, sleep apnea, susceptibility to complications of respiratory infections etc.
MONITORING: Blood gas assessment once in first few weeks of life. Polysomnography in first 6 months of life.
INTERVENTION: Aggressive treatment of lower respiratory infections. Use of oxygen, cpap, bipap, tracheostomy, ventilator support etc. may be required, as indicated by polysomnography and clinical course.

PROBLEM: **ANESTHETIC MANAGEMENT**
EXPECTATIONS: There is a high probability that general anesthesia will be needed for surgical intervention(s). Risks relate primarily to cervical spine instability, midface retrusion which makes intubation even more challenging, limited respiratory reserve, and markedly small airways.
MONITORING/INTERVENTION: Assess cervical spine stability before any anesthesia and, if unstable or uncertain, intubation should be completed by bronchoscopic visualization with external neck stabilization. Insure that appropriately small endotracheal tubes are available (e.g. premie sizes for young children, pediatric size even when caring for adults). Anticipate that delayed extubation may be needed given limited respiratory reserve.

PROBLEM: **ADAPTIVE**
EXPECTATIONS: There will be considerable psychological and physical adaptive needs later in childhood.
MONITORING: Assess for age appropriate needs.
INTERVENTION: Examples include reachers, adaptations for toileting, school adaptations, stools, teacher involvement, Little People of America involvement.

GENETICS AND MOLECULAR BIOLOGY

Spondyloepiphyseal Dysplasia, Congenita appears always to be caused by an autosomal dominant gene abnormality. This means that an adult with this disorder will have a 50% chance to pass this poorly functional gene on to each child. Not infrequently an individual with this disorder will be born to average statured parents; when this happens it arises because of a new chance change (mutation) in only the single egg or single sperm giving rise to the affected individual. Although instances of germinal mosaicism have been recognized rarely, overall this

means that average statured parents who have had one child with this disorder have no significant risk for it to recur in subsequent children.

Spondyloepiphyseal Dysplasia, Congenita is one of a group of bone and cartilage disorders that are termed *Type II Collagenopathies.* That is, each member of this group of disorders (that also includes, e.g. Stickler syndrome, Kniest dysplasia, Spondyloepimetaphyseal dysplasia, certain forms of Achondrogenesis etc.) arises because of changes in the synthesis of type II collagen, coded for by the *col2A1* gene. Type II collagen is particularly important in the connective tissues of joints, in bone growth, in the airways and in the development of the eye.