INTRODUCTION:

The following summary of the medical expectations in Achondroplasia 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 young children with this disorder, and particularly to help clinicians caring for a recently diagnosed child. It is limited to those problems that are likely to be encountered in the first few years of life. 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].

Achondroplasia is the most common of the bone dysplasias, arising in around 1 in every 25,000 individuals. Well defined clinical and radiologic criteria for diagnosis are available. In infancy, clinical features include disproportionate, shortened limbs (shortened more in the upper segments), short fingers, enlarged head, depressed nasal bridge and a somewhat constricted chest. Radiographs are usually diagnostically definitive.

Additional guidelines for care are available through the American Academy of Pediatrics.

MEDICAL ISSUES AND PARENTAL CONCERNS TO BE ANTICIPATED

PROBLEM: LIFE EXPECTANCY

EXPECTATIONS: Most individuals with achondroplasia can be expected to have a normal life expectancy. However, mortality studies have shown that infants and children under 2 years of age have some increased risk for death. Best estimates are that, without careful assessment and intervention, between 2% and 5% of children with achondroplasia will die. Nearly all of this risk is secondary to craniocervical junction abnormalities (see below).

MONITORING: See below under Craniocervical Junction Associated Risks.
INTERVENTION: See below under **Craniocervical Junction Associated Risks.**

**PROBLEM: GROWTH**

**EXPECTATIONS:** There is moderate to marked short stature, with a fairly narrow range of ultimate adult height between about 3 feet 8 inches and 4 feet 9 inches (112-145 cm). Mean adult height is around 4’3” in males and 4’1” in females.

**MONITORING:** Monitor growth using achondroplasia-specific growth grids. There are also achondroplasia-specific weight, weight-by-height and BMI grids that should be used to monitor ponderal growth.

**INTERVENTION:** There is no known specific treatment for the growth abnormality. Growth hormone trials show only very limited effect as would be anticipated since this disorder is secondary to intrinsic abnormality of bone growth. Limb lengthening is chosen by a small minority of affected individuals. Extended limb lengthening is a complex process and, if chosen, should only be performed in a multidisciplinary setting. When done in the United States, in general, extended limb lengthening is performed in teenage years.

**PROBLEM: HEAD GROWTH AND RISK FOR HYDROCEPHALUS**

**EXPECTATIONS:** Nearly all children have large heads. In most this is secondary to benign ventriculomegaly and excess extraaxial fluid accumulation. About 5% of children with achondroplasia will develop symptomatic hydrocephalus requiring shunting.

**MONITORING:** All should have baseline neuroimaging in infancy to assess ventricle size and volume of extraaxial fluid. All should have serial head circumferences every 1 to 2 months in the first year of life and then with each physician contact thereafter. Measures must be plotted on achondroplasia-specific grids. Parents should be taught to watch for signs of increased intracranial pressure.

**INTERVENTION:** Repeat neuroimaging if head growth acceleration or signs/symptoms of hydrocephalus arise. Ventriculoperitoneal shunting should only be performed for symptomatic hydrocephalus.

**PROBLEM: CRANIOCERVICAL JUNCTION ASSOCIATED RISKS**

**EXPECTATIONS:** All have craniocervical junction constriction secondary to a small foramen magnum. Risk of death from this complication is probably 2-5% secondary to damage to lower medullary respiratory control centers and consequent central apnea; this is almost exclusively a risk of the first year of life. In addition, acute or chronic damage to the upper cervical cord can result in neurologic damage (high cervical myelopathy).

**MONITORING:** Complete careful clinical neurologic assessments in infancy. Neuroimaging should be done in early infancy in every affected child. (Computerized tomography of the craniocervical junction allows precise measurement of the foramen magnum [with comparison to achondroplasia-specific standards of foramen magnum size] and often can be completed without sedation. Magnetic resonance imaging allows better delineation of neural structures but nearly always requires sedation or anesthesia.) Polysomnography should be completed in early infancy, as well.

**INTERVENTION:** Parental counseling regarding careful neck support with handling, using a solid-back stroller and baby-safe, avoidance of umbrella strollers, swing-o-matics, and Johny-jump-ups. In those who are symptomatic or judged to be at very high risk, neurosurgical suboccipital
decompression is needed. This is likely necessary in about 8-10% of all children with achondroplasia. Because of risks associated with craniocervical stenosis, all older children should have certain activity prohibitions, including prohibition of collision sports, vaulting, use of a trampoline etc.

**Problem: Respiratory Problems in Infancy**

**Expectations:** As noted, central apnea (that may be life-threatening) may arise secondary to craniocervical junction constriction. In addition, some infants have sufficiently constricted chests (and overly compliant ribs) to have restrictive pulmonary problems.

**Monitoring:** Chest circumference measurements can be compared with achondroplasia specific standards. Clinical assessments should assess for signs of respiratory distress. Continuous nighttime oximetry will be obtained as part of polysomnography. Daytime continuous or spot oximetry may be warranted if clinical concerns arise.

**Intervention:** Transient oxygen supplementation will be needed in a small minority.

**Problem: Obstructive Apnea**

**Expectations:** Although very infrequent in infancy, obstructive sleep apnea is exceedingly common between 2 years and 10 years of age. Many factors can contribute to this risk including intrinsically small airways, redundant pharyngeal soft tissue and (physiologic) hypertrophy of adenoids and tonsils; obesity can also be a potent contributing factor. If left untreated, obstructive apnea can result in chronic hypoxemia and secondary pulmonary hypertension and heart changes.

**Monitoring:** Snoring is virtually uniform and probably does not in itself indicate clinically significant airway obstruction. Parents should be taught to monitor for additional signs and symptoms of obstruction, including neck hyperextension, loud snoring, glottal stops, apneic pauses, compensatory sighs, self arousals, newly developing enuresis, nighttime vomiting, daytime irritability or sleepiness etc. If suspicions of serious obstructive apnea arise, then polysomnography should be repeated.

**Intervention:** Depending of severity of obstruction and response to treatment, options can include adenoidectomy, tonsillectomy, cpap or bipap, uvulectomy, uvulopharyngopalatoplasty, tracheostomy. Only around 1-2% will have sufficiently refractory obstruction to require tracheostomy. In nearly all of those, tracheostomy need is transient.

**Problem: Ears and Hearing**

**Expectations:** A majority of infants and young children with achondroplasia will develop recurrent or persistent middle ear dysfunction with conductive hearing loss. If not aggressively treated, this may contribute to delays in language and speech development. Middle ear dysfunction is often resistant to medical management.

**Monitoring:** Behavioral audiometric and tympanometric assessment should be completed, first at 9-12 months of age and every 9-12 months throughout early childhood. There should be a high level of suspicion that middle ear problems are present.

**Intervention:** Aggressive use of myringotomy and pressure equalizing tube placement. If a child needs ventilating tubes, then they should be maintained until 6-8 years of age, since only...
then will most children with achondroplasia develop Eustachian tube autonomy.

**Problem: Kypnosis**  
*Expectations:* Most infants develop a flexible kyphosis. A minority have progressive kyphotic deformity of the thoracolumbar junction. If untreated, around 10% will develop anterior wedging and a fixed angular curve that can result in neurologic deficits in adolescence or adulthood secondary to cord tethering.  
*Monitoring:* Clinical assessment. If a significant non-reducible curve develops, radiologic assessment (sitting lateral and either cross-table prone lateral or cross-table supine over a bolster lateral x-rays of the thoracolumbar spine) should be obtained.  
*Intervention:* Prohibition of unsupported sitting in the first 12-14 months, along with emphasis on good back support, lots of prone position activities and limiting disadvantageous positioning (i.e. in a trunk-flexed position) markedly reduces the risk of progressive deformity. If a fixed curve of greater than 30° nonetheless develops, then TLSO bracing will need to be initiated.

**Problem: Lordosis**  
*Expectations:* All children will develop hyperlordosis and a prominent, horizontal sacrum with the assumption of orthograde posture. If particularly severe, it may result in chronic pain and increased risk for symptomatic spinal stenosis later in life.  
*Monitoring:* Clinical assessment.  
*Intervention:* If severe, physical therapy to teach parents and the child an exercise regimen including stretching of hip flexors, lower abdominal muscle strengthening, paraspinous strengthening and 'tucking under' is appropriate. This never requires either bracing or surgical intervention.

**Problem: Limited Elbow Extension**  
*Expectations:* Limitation ranging from 20° to 60° short of full extension is common. When present this may further limit functionally effective reach (e.g. for toileting).  
*Monitoring:* Clinical assessment.  
*Intervention:* Use of adaptive devices (e.g. bottom wiper) as needed.

**Problem: Wrist Hypermobility**  
*Expectations:* Wrists are usually hypermobile, sometimes markedly so. When particularly marked, failure to adequately stabilize the wrist can result in fine motor difficulties, excess fatigability from drawing or writing etc.  
*Monitoring:* Clinical assessment of degree of hypermobility and its effects on fine motor endurance should be completed.  
*Intervention:* In some either environmental modifications (e.g. of eating utensils, writing implements etc.) or use of a small, lightweight wrist stabilizing brace may be needed. Occasionally, writing is sufficiently problematic that early transitioning to keyboarding is appropriate.
**PROBLEM:** **Knee Instability**  
**Expectations:** Both genu recurvatum and mediolateral instability are virtually constant, but with markedly variable severity. Occasionally, young children will have tibial-femoral subluxation with full extension. Instability contributes to delays in gross motor development. Often, the need for voluntary muscle stabilization will result in harmless pain associated with prolonged standing and walking.  
**Monitoring:** Clinical assessment.  
**Intervention:** Usually this will require no intervention. Infrequently instability will be so severe that stabilization using KAFOs may be needed transiently. Rarely flexion osteotomies may be required to effect long term stabilization.

**Problem: Varus Deformity**  
**Expectations:** Progressive varus at the knees and of the mesial segments of the legs is exceedingly common, probably affecting 60-80% of all children. In fact, “bowing” is usually not just lateral deformity, but also includes internal tibial torsion and mediolateral knee instability when the child is orthograde.  
**Monitoring:** Clinically monitor for position and determination if the three weight-bearing joints of the leg remain in plumb. In addition, symptoms that should be sought include activity-precipitated pain, decreased endurance for walking and running, and decreased activity level.  
**Intervention:** If joints become significantly out of plumb or if position is associated with marked pain, then surgical intervention is needed. Usually correction is by proximal tibial and fibular valgus and derotational osteotomies, with either internal or external fixation. Fibular epiphysiodesis is probably not a reasonable alternative surgical method. Use of 8-plates may be of benefit if an individual has relatively pure varus without significant torsional deformity.

**Problem: Development**  
**Expectations:** Cognitive abilities are normal unless complications intervene. The combination of hypotonia, large head, short limbs and joint hypermobility results in delays and unusual patterns of gross and fine motor development.  
**Monitoring:** Assessment of development should be by comparison with achondroplasia specific norms and known differences of patterns of motor development.  
**Intervention:** Usually only reassurance is needed.

**Problem: Adaptive**  
**Expectations:** Considerable psychological and physical adaptive needs may arise later in childhood.  
**Monitoring:** Assess for age appropriate needs.  
**Intervention:** School adaptations, stools, adaptations for toileting, teacher involvement, Little People of America (LPA) involvement.
Achondroplasia is always 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 (although special risks are present if both parents are affected). Not infrequently an individual with this disorder will be born to average statured parents. When this happens it is because of a new chance change (mutation) in only a single germinal cell giving rise to the affected individual. This means that the risk for recurrence in a next pregnancy is virtually zero. The gene change for achondroplasia is fully penetrant (never ‘hidden’).

All instances of achondroplasia arise because of a specific mutation of one gene – the FGFR3 gene. Remarkably, virtually always is arises from the identical nucleotide substitution at the same site in the FGFR3 gene. FGFR3 codes for a protein essential for recognition of growth stimuli and signal transduction in those cells normally stimulated. This growth factor receptor appears to be particularly crucial in cartilage and bone growth.

Although readily available, FGFR3 testing is usually not needed. It should be reserved for those rare instances in which diagnosis is in doubt.